DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00010-11 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Noninvasive Assessment of the Left Ventricle in Normal Man

PRINCIPAL INVESTIGATOR *(List other professional personnal below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | J. L. Fleg | Staff Cardiologist | CPB, NIA |
| Others: | E. G. Lakatta | Chief, Cardiovascular Section | CPB, NIA |
| | E. S. Beard | Chemist | CPB, NIA |

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.8 | 0.03 | 0.05 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

To define the prevalence of coronary artery disease (CAD), both overt and latent, in a free-living population, we have performed exercise thallium scintigraphy in collaboration with the Johns Hopkins University, Division of Cardiology in approximately 500 individuals from the BLSA. Preliminary analysis of these data has shown an age-related increase in the prevalence of both overt and latent CAD. We have also found that the incidence of subsequent coronary events (angina, myocardial infarction or cardiac death) in asymptomatic subjects is strikingly high in the subset whose thallium scan and exercise ECG are both abnormal.

We have also used thallium scintigraphy and exercise ECGs to define a group of men and women ostensibly free from CAD in whom left ventricular function has been measured during maximal bicycle exercise by radionuclide angiography (MUGA), also in conjunction with Johns Hopkins. In these carefully selected subjects, maximal cardiac output did not decline with age -- contrary to the body of literature in less intensively screened individuals. Nevertheless, the methods of achieving maximal cardiac output were found to differ with age, the young attaining a more rapid heart rate and more complete systolic emptying, whereas the elderly depended more upon the Frank-Starling mechanism, i.e. dilation of the heart during the filling period. Although maximum diastolic filling rate at rest declined with age, no such age relationship was seen during exercise at a 100 watt workload. Thus, the age-related diminution in early diastolic filling rate at rest which has been documented in the BLSA population both by echocardiographic and radionuclide techniques, does not appear to limit diastolic filling during exercise.

Discontinued.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00011-12 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Hormones and aging. I. Adenylate cyclase and hormone action.

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.I. Gregerman, Chief, Endocrinology Section, Clinical Physiology Branch, NIA

COOPERATING UNITS *(if any)*

Department of Surgery, Francis Scott Key Medical Center
Oncology Center, Johns Hopkins Hospital

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Endocrinology Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| | | |

CHECK APPROPRIATE BOX(ES)

- [X] (a) Human subjects
  - [ ] (a1) Minors
  - [ ] (a2) Interviews
- [X] (b) Human tissues
- [ ] (c) Neither

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The project includes studies on the biochemistry of hormone-sensitive adenylate cyclase in a variety of tissues. Their purpose is to explore the mechanisms by which age produces alterations of hormone-responsiveness in biological membranes, with special emphasis on the relationship between adenylate cyclase and hormone receptors. Dietary effects on the components of the adenylate cyclase system are also under study. The mechanism of the age-related decrease of catecholamine- sensitive lipolysis is being studied in comparative measurements in two strains of rat (GRC-Wistar and Fisher 344) which exhibit different age-related changes. Aging in fat cells is being studied in tissue culture of pre-adipocytes from these rats. The phenomenon of stress-related inhibition of thyrotropin (TSH) secretion and development of low thyroxine ($T_4$) in severely ill humans ("euthyroid sick syndrome") is under study.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00013-10 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 charecters or less. Title must fit on one line between the borders.)*

Hormones, hormone receptors, and aging. III. Aging and human endocrine regulation.

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

S. M. Harman, Senior Investigator, Clinical Physiology Branch, NIA

COOPERATING UNITS *(if any)*

Developmental Endocrinology Branch, NICHD, NIH
Department of Medicine, Francis Scott Key Medical Center

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Endocrinology and Human Performance Sections

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.6 | 1.4 | 0.2 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

These studies gather data on pituitary function as it relates to gonadal, thyroid, adrenal, and growth hormone regulation in normal aging men from the Baltimore Longitudinal Study on Aging (BLSA). Recent results have shown that healthy men have changes in pituitary secretion of thyroid stimulating hormone (TSH) which are quite minimal and no apparent change in growth hormone secretion compared with the decrements of secretory capacity reported for less well selected populations.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00015-26 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

The Baltimore Longitudinal Study of Human Aging

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

See Attached Page.

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Human Performance Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| | | |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The Baltimore Longitudinal Study of Human Aging (BLSA) serves as a resource for scientists working in the field of Gerontology. It provides a well-described group of men and women between 20 and 96 years of age for studies of the mechanisms of human aging. Projects in physiology, biochemistry, psychology, nutrition, pharmacology, endocrinology, sociology, and genetics, have been carried out or are in progress.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00018-18 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Marital, Sexual and Social Factors in Aging.

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C. Martin Sociologist CPB NIA

COOPERATING UNITS *(if any)*

Paul Ephross School of Social Work and Community Planning, University of Maryland at Baltimore

Jan D. Sinnott Dept. of Psychology, Towson State University

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Human Performance Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| | | |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Dr. Martin, the principal investigator, has retired and data is no longer being collected. The data is currently being analyzed by his collaborators and manuscript on relationship to benign prostatic hypertrophy is being prepared.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 AG 00021-21 CPB

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Study of Normal Human Variability

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
*(Name, title, laboratory, and institute affiliation)*

C.C. Plato Sr. Research Geneticist CPB NIA

COOPERATING UNITS *(if any)*

See attached page.

LAB/BRANCH
Gerontology Research Center, Clinical Physiology Branch

SECTION
Human Performance Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.00 | 0.40 | 0.60 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Dermatoglyphics, the development and final configurations of digital and palmar dermal ridges have proven to be excellent biological markers. While they are for the most part genetically determined, their final development, which is completed at the end of the first trimester of pregnancy, is also influenced by intrauterine disturbances. Once developed, dermatoglyphics do not change nor can they be altered. No two individuals (including identical twins) have identical dermatoglyphics. These qualities make dermatoglyphics very useful genetic, as well as early prenatal enviromental markers in clinical studies.

This project represents an ongoing collaborative effort, involving WHO and other national and international laboratories to coordinate the collection, evaluation and interpretation of normal genetic markers. Specifically, the objectives of this project are: (A) To study the distribution of Dermatoglyphic markers in population isolates, family units, disease entities and normal control samples, and to utilize these genetic markers in understanding the etiology, development and early diagnosis of diseases or processes with late onset. (B) To determine the lateral functional dominance, grip strength, among BLSA participants, and assess their relationship to physiological processes or diseases demonstrating bilateral asymmetry. (C) Cross-sectional and longitudinal study of visual function in BLSA participants.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00023-09 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 charecters or less. Title must fit on one line between the borders.)*

Hormones and aging. Pituitary, and hypothalamic function in experimental animals.

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

S. M. Harman, Senior Investigator, Clinical Physiology Branch, NIA

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Endocrinology Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, MD 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.0 | 1.4 | 0.6 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Usa standard unreduced type. Do not exceed tha spaca provided.)*

Secretory cells from rat pituitaries are studied in vitro to compare their physiology in old and young animals. Production of TSH and prolactin in response to TRH and production of LH and FSH and their subunits in response to LRH are being measured in order to investigate altered function of pituitary secretory cells. Deranged function of aged pituitary cells in vitro has been found. Castration increases LRH responsiveness of gonadotrophs of aged and young rats to the same extent. Pretreatment of rats with LRH has partially restored LH secretory function of cells from old animals, suggesting that hypothalamic deficiency is, at least in part, responsible for the observed age-related reduction in LH secretion.

DEPARTMENT OF HEALTH AND HUMAN SERVICES · PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 AG 00022-08 CPB

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Investigations of Osteoarthritis and Bone Loss

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
*(Name, title, laboratory, and institute affiliation)*

C.C. Plato Sr. Research Geneticist CPB NIA

COOPERATING UNITS *(if any)*
Laboratory of Central Nervous System Studies, NINCDS

LAB/BRANCH
Gerontology Research Center, Clinical Physiology Branch

SECTION
Human Performance Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.0 | 0.95 | 0.95 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Osteoarthritis and bone loss are the two principal age related changes of the human skeleton. Even though these changes are considered inherent to aging, they may result in incapacitation ailments. Bone loss and osteoarthritis are universal phenomena. The advanced cases of osteoarthritis (degenerative joint disease) produce severe restrictions of movement associated with pain. Advanced bone loss may result in osteoporosis and frequent bone fractures. At some time during the fourth decade of life the human skeleton begins to loose bone. That is, bone mass decreases in relation to bone volume. In tabular bones, bone is resorbed from the endosteal surface. Because of the thinning of the cortical bone shell, bones loose their mechanical integrity and fracture more readily. The trabecular bone mass of the verteral column also decreases with age. The vertebral plates decrease in density, loose resistance to vertical compression stress and are more vulnerable to vertebral collapse. Most prominent are vertebral compression fractures and fractures of the femoral neck. The following skeletal sites are involved in the present study: hand-wrist, ulna and radius and vertebral column. This project deals with the epidemiological, genetic and longitudinal aspects of osteoarthritis and bone loss among (1) the participants of the Baltimore Longitudinal Study, (2) in a sample of normal children and adult Guamanians (Chamorros), (3) among patients afflicted with Amyotrophic Lateral Sclerosis/Parkinsonism Dementia Complex of Guam, and 4) study of bone mineral density and effect of muscular activity on bone in rats.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 AG 00028-08 CPB

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Epidemiological & Genetic Studies of ALS/PD Complex of Guam

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
*(Name, title, laboratory, and institute affiliation)*
C.C. Plato Sr. Research Geneticist CPB NIA

COOPERATING UNITS *(If any)*
C & F Research Center, NINCDS

LAB/BRANCH
Gerontology Research Center, Clinical Physiology Branch

SECTION
Human Performance Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MANYEARS: | 0.50 | PROFESSIONAL: | 0.20 | OTHER: | 0.30 |
|---|---|---|---|---|---|

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In an effort to elucitate the etiology of high incidence of ALS and PD on the island of Guam, a patient-control prospective study (Registry) was established in 1958. The Registry includes, in addition to the patients and their individually matched controls, their respective parents, sibs, offspring and spouses. The objective of the registry has been to determine (1) whether relatives of ALS and PD patients have higher risk for developing the disease than relatives of controls and (2) if familial occurrence does exist, to determine the extent of genetic involvement in the etiology of the disease. A twenty-five year follow-up analysis of the registry has just been concluded.

Other objectives of this study are: 1) to investigate the genetic and epidemiological factors contributing to the very high incidence of Amyotrophic Lateral Sclerosis and Parkinsonism Dementia (ALS/PD) on Guam; 2) to evaluate the distribution of the various estalished genetic and anthropological markers among the normal Guamanian population and compare them with those of the ALS/PD patients; and 3) to acertain the effects of immobilization due to paralysis on bone density.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00029-07 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Efficacy of Digitalis in Congestive Heart Failure and in Normal Subjects

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | J. L. Fleg | Staff Cardiologist | CPB, NIA |
| Others: | E. G. Lakatta | Chief, Cardiovascular Section | CPB, NIA |

COOPERATING UNITS *(if any)* Division of Cardiology, Francis Scott Key Medical Center, Baltimore, MD (S. H. Gottlieb), Peter Bent Brigham Hosp., Boston, MA (Thomas Smith), University of Arizona, Tucson, AZ (Frank Marcus), Massachusette General Hospital, Boston, MA (Robert Johnson), Duke University, Durham, NC (Harold Strauss)

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.4 | 0.2 | 0.2 |

CHECK APPROPRIATE BOX(ES)

☒(a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have previously shown in a double-blind crossover study that digitalis could be discontinued for three months without adverse clinical effect and only minor changes in cardiac size and function in 30 subjects with stable congestive heart failure (CHF) and sinus rhythm. Long-term folow-up of these patients verified this favorable early response to digitalis withdrawal. We have initiated a new study to investigate the effects of digitalis on aerobic performance and cardiac function during exercise (measured via gated blood pool scan) and its effects on cardiac rhythm in a new group of patients with chronic CHF and sinus rhythm.

Our group has helped to develop a questionnaire in conjunction with experts in cardiology at different universities. This questionnaire has been implimented with the help of the American Heart Association to sample representative groups of academic and practicing physicians in their current use and understanding of the effectiveness and toxicity of digitalis glycosides. The results will be important in identifying areas of consensus and areas in which major uncertainties exist; the important categories within the latter will serve as a basis for future research projects in which NIH and NIA may find a direct role.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00033-06 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Ambulatory Electrocardiography and Blood Pressure Measurement in Normal Man

PRINCIPAL INVESTIGATOR *(List other professionel personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | J. L. Fleg | Staff Cardiologist | CPB, NIA |
| Others: | E. G. Lakatta | Chief, Cardiovascular Section | CPB, NIA |

COOPERATING UNITS *(if any)*

Saint Louis University School of Medicine, St. Louis, MO (H. J. Kennedy)

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.3 | 0.5 | 0.8 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Initial ambulatory electrocardiographic data from this laboratory has characterized the normal heart rhythm patterns in healthy elderly subjects. We have extended these efforts to include younger men and women (ages 25-60). In addition, we have added a new dimension - 24 hour ambulatory blood pressure (BP) recording - simultaneous with the ambulatory ECG recording, in normal subjects as well as hypertensives and those with congestive heart failure.

We have analyzed the circadian variability of blood pressure, recorded every 7.5 min, over 24 hours in 26 healthy normotensive BLSA women ages 35-75 yuears using this technique. Both the mean waking systolic blood pressure (SBP) and its standard deviation increased with age whereas during sleep, the mean SBP but not its standard deviation increased with age. The difference between maximum and minimum hourly-averaged waking SBP increased with age whereas the difference during sleep was not age-related. Thus, in ambulatory, normotensive women, the variability of SBP increased with age during waking hours but not during sleep.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00035-05 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Fluctuations in the Intensity of Light Scattered through Diastolic Cardiac Muscle

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | | |
|---|---|---|---|---|
| PI: | E. G. Lakatta | Chief, Cardiovascular Section | | CPB, NIA |
| Others: | A. A. Kort | Medical Staff Fellow | DOD 06/30/84 | CPB, NIA |
| | G. M. Bhatnagar | Guest Researcher | | CPB, NIA |
| | M. D. Stern | Expert | | CPB, NIA |

COOPERATING UNITS *(if any)*

Cardiology Division, Department of Medicine, Johns Hopkins Hospital, Baltimore, MD (E. Marban), Department of Physiology, University of Maryland, Baltimore, MD (W. G. Wier)

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.8 | 2.7 | .1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have discovered that scattered light intensity fluctuations (SLIF) are present in isolated rat ventricular muscle even under conditions formerly considered to be quiescent. Subsequent experiments indicated that SLIF are highly dependent on calcium loading of the cell and could be reversibly terminated (1) by maintaing constant calcium concentration in the myofilament space in skinned fibers or (2) in intact fibers by caffeine. These results were interpreted to indicate that cellular myoplasmic calcium concentration oscillates in diastole, producing motion of the myofilaments, which modulates the laser beam and results in SLIF. This myofilament motion which is asynchronous within a cell, and among cells, results in a small degree of diastolic force or "tone" in the muscle. Additional experiments have demonstrated SLIF in atrial, ventricular, and conduction tissues in a range of mammalian species including man and indicate the universality of this phenomenon in excitable cardiac tissues. In collaboration with the Department of Physiology at the University of Maryland, we have directly demonstrated these $Ca^{2+}$ oscillations utilizing intracellular injects of the chemiluminescent protein, aequorin. In our most recent studies we have time gated SLIF measurements in a diastolic window following stimulation in order to determine the effects of stimulation on calcium loading and to determine whether certain antiarrhythmic drugs used to treat $Ca^{2+}$-dependent arrhythmias had an effect on post stimulation SLIF. We found that stimulation increases SLIF frequency in this diastolic window and that anti-arrhythmias suppress this increase.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00036-04 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Interaction of Age and Physical Conditioning on Myocardium and Vasculature

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | H. A. Spurgeon | Physiologist | CPB, NIA |
| Others: | E. G. Lakatta | Chief, Cardiovascular Section | CPB, NIA |
| | E. S. Beard | Chemist | CPB, NIA |
| | M. F. Steinbach | Biologist DOD 1/31/84 | CPB, NIA |
| | M. B. Effron | Senior Staff Fellow | CPB, NIA |

COOPERATING UNITS *(if any)*

Division of Cardiology, Department of Medicine, Johns Hopkins Hospital, Baltimore, MD (F. C. P. Yin)

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.0 | 0.5 | 1.5 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Our laboratory has previously shown that aging affects myocardial function in rats, specifically that parameters measuring the duration of the isometric twitch increase with age. It has also been shown that myofibrillar ATPase Activity as well as responsiveness of vascular smooth muscle (VSM) to adrenergic agents decrease as the animal ages. Short term physical conditioning reversed the changes in myocardial performance seen in the senescent heart in rats. Because of the emphasis of exercise in relationship to health, we designed a chronic exercise model in the rat to evaluate the relationship between exercise and aging. A swimming model has been developed in which daily swimming is begun in rats 5 weeks of age and continued for the duration of their lives. We have been able to obtain adequate survival to 18 months of age with isolated survivors beyond that time. Mortalities, commonly during swimming, have been analyzed as to the effect of chronic exercise on body weight and heart size. Preliminary analysis of the oldest age group shows no difference in baseline twitch characteristics but there is a trend for an increase response to catecholamines in the exercise animals. Maximal myofibrillar ATPase activity was slightly although significantly higher in the oldest exercised animals. Exercise did not appear to alter the $ED_{50}$ of norepinephrine on VSM in any age group while the oldest animals from the exercised group showed a greater response to alpha-adrenergic stimulation of VSM compared to age matched controls. Studies are continuing on the animals across a wide age range to evaluate the effect of lifelong exercise on myocardial and VSM function as well as myofibrillar ATPase activity.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00037-04 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Adaptation of Cardiac Muscle to Chronic Volume Overload is Altered by Age

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | | |
|---|---|---|---|---|
| PI: | G. D. Walford | Staff Fellow | DOD 7/01/83 | CPB, NIA |
| Others: | E. G. Lakatta | Chief, Cardiovascular Section | | CPB, NIA |
| | E. S. Beard | Chemist | | CPB, NIA |

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| | | |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Our model is the male rat subjected to chronic complete heart block at two different ages, 5 and 12 months, compared to age-matched control. We studied the response of contractile proteins to calcium by disrupting cell membrances to isolated muscle strips with the non-ionic detergent Triton X-100 and then determining calcium dose-response curves for force development. Our results indicate that significantly more contractile force per unit of muscle area is developed by young, compared to older, animals with heart block or to control animals of either age. Thus an interaction of age and chronic volume overloading of the heart by complete heart block is demonstrated.

Discontinued.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00038-03 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Evaluation of Peripheral Blood Flow in Normal Man by Plethysmography

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | J. F. Fleg | Staff Cardiologist | CPB, NIA |
| Others: | E. G. Lakatta | Chief, Cardiovascular Section | CPB, NIA |
| | E. S. Beard | Chemist | CPB, NIA |

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| .60 | .30 | .30 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Although the incidence of degenerative changes in the blood vessels is well known to increase with advancing age, quantitative data on the changes in peripheral blood flow due to the aging process per se are lacking. Venous occlusion plethysmography has been shown to be the most accurate and reproducible method to measure the peripheral blood flow. We used this method to evaluate peripheral blood flow in the subjects of the Baltimore Longitudinal Study of Aging (BLSA) with ages ranging from 20 to 83 years. The study was designed to evaluate the effect of age on peripheral blood flow by venous occlusion plethysmography at rest and in response to post-occlusion hyperemia and thermal stress, both of which result in near-maximal flow. Neither resting nor post-occlusion hyperemic blood flow as relate to age in these 146 BLSA men and women who underwent occlusions of 1, 2, and 3 minutes both at 26°C and 35°C. These results suggest that peripheral blood flow is not limited by age per se in man.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00039-03 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Long-term Prognosis of Asymptomatic Men with Complete Right Bundle Branch Block

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | J. L. Fleg | Staff Cardiologist | CPB, NIA |
| Others: | E. G. Lakatta | Chief, Cardiovascular Section | CPB, NIA |

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.3 | 0.3 | |

CHECK APPROPRIATE BOX(ES)

☒(a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The long-term cardiac prognosis of 24 clinically healthy men with complete right bundle branch block (RBBB), identified from the 1140 men constituting the BLSA population, was assessed over a follow-up period averaging 8.4 years. When compared with a control group matched or age at which RBBB appeared, men with RBBB showed no difference in the prevalence of antecedent coronary risk factors or obstructive lung disease. Their incidence of angina pectoris, myocardial infarction, valvular heart disease, cardiomegaly, congestive heart failure, advanced heart block, or cardiac death did not differ from that of the control group over the observation period. Furthermore, at latest follow-up maximal aerobic exercise tolerance and chronotropic response to maximal exercise were not impaired in men with RBBB relative to controls. However, axis deviation leftward of -30° was present in 46% of RBBB men but only 15% of controls by latest follow-up. Although a PR interval prolongation greater than 40 msec developed in only 6% of control subjects over the observation period, such prolongation occurred in 29% of men with RBBB. These results support the concept that RBBB in these asymptomatic men is a manifestation of a primary abnormality of the cardiac conduction system but has no demonstrable adverse effect.

Combined into Z01 AG 00228-01 CPB.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00043-11 LMA

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Regulation of Intermediary Metabolism

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | |
|---|---|---|
| Richard G. Hansford | Research Chemist | LMA, GRC, NIA |
| Other: | | |
| B. Ashour | Visiting Fellow | LMA, GRC, NIA |
| F. Castro | Chemist | LMA, GRC, NIA |

COOPERATING UNITS *(if any)*

None

LAB/BRANCH
Gertontology Research Center, Laboratory of Molecular Aging

SECTION
Intermediary Metabolism Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.1 | 1.1 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project involves the description of the basic mechanisms whereby energy metabolism is controlled, and the pertubations in these mechanisms that occur in old-age. Work has focussed on the role of the calcium ion in regulating pyruvate dehydrogenase activity in brain mitochondria and this has relevance to the synthesis of neurotransmitter substances. The study has involved both experiments with isolated mitochondria, in which the pCa of the medium is varied, and experiments with synaptosomes, in which cytosolic free calcium ion concentration is elevated indirectly, by depolarization of the plasma membrane. This mimics the excitation of nerve and leads to increases in the active form of pyruvate dehydrogenase. Cytosolic free calcium concentrations have been measured directly in these studies by the use of the fluorescent chelating agent Quin-2. Responses of both the pyruvate dehydrogenase system and of Quin-2 fluorescence to the inhibitors ouabain, KCN, oligomycin and ruthenium red have been investigated, in order to assign quantitative significance to the role of calcium ions and to adenine nucleotides in mediating between membrane depolarization and dehydrogenase activation. Other studies have focussed on calcium transport by brain mitochondria by both electrogenic uptake and electroneutral release pathways.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00044-11 LCMB

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Effect of Metals and Proteins on Nucleic Acid, Information Transfer and Aging

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | Gunther L. Eichhorn | Chief, LCMB | IBS LCMB NIA |
| Others: | James J. Butzow | Commissioned Officer | IBS LCMB NIA |
| | Patricia Clark | Research Chemist | IBS LCMB NIA |
| | Robert E. Monticone | Biologist | IBS LCMB NIA |
| | Yong A. Shin | Research Chemist | IBS LCMB NIA |
| | Rajasekharan P. Pillai | Visiting Associate | IBS LCMB NIA |
| | Edward Tarien | Chemist | IBS LCMB NIA |
| | Daniel Waysbort* | Visiting Associate | IBS LCMB NIA |
| | Mordechai Chevion** | Visiting Associate | IBS LCMB NIA |

COOPERATING UNITS *(if any)*
Laboratory of Molecular Biology, NIADDK (E. Charney, I. Levin, S. Zimmerman.
Department of Chemistry, Wichita State University (R. Singhal).

LAB/BRANCH
Laboratory of Cellular and Molecular Biology

SECTION
Inorganic Biochemistry Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 5.6 | 4.6 | 1.0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This projects focuses on the interaction of molecules concerned with genetic information transfer. A primary objective is to determine under what conditions metal ions are essential for information transfer, and under what conditions they produce errors in the information and may thus contribute to biological aging. Topics of interest are: (1) the effects of metal ions on the structure of nucleic acids, nucleoproteins and chromatin; (2) the mechanism of involvement of aluminum in Alzheimer's disease; (3) crosslinking of nucleic acid strands by metal ions; (4) the effects of metal ions on RNA polymerase; (5) metal ions and cellular aging.

*On leave from Israel Institute for Biological Research, Ness-Ziona
**On leave from Hebrew University Medical School, Jerusalem

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 AG 00046-14 LCMB

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)
Medicinal Chemistry Applied to Problems Prominent in Senescence

PRINCIPAL INVESTIGATOR (List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)

| | | | |
|---|---|---|---|
| PI: | Josef Pitha | Section Chief | MCS LCMB NIA |
| Others: | John Kusiak | Research Chemist | MCS LCMB NIA |
| | Grzegorz Blotny | Visiting Associate | MCS LCMB NIA |
| | Andras Liptak | Visiting Associate | MCS LCMB NIA |
| | Zoltan Szurmai | Visiting Fellow | MCS LCMB NIA |

COOPERATING UNITS (if any)
University of Florida, J. Hillis Miller Health Center, Gainesville, Florida; University of Minnesota, Minneapolis, Minnesota; NIDR, NIH, Bethesda, Maryland; University of San Francisco, San Francisco, California.

LAB/BRANCH
Laboratory of Cellular and Molecular Biology

SECTION
Macromolecular Chemistry Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 4.75 | 4.75 | 0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

The skills of pharmacologists and chemists can help physicians' efforts to treat diseases prominent in aging. The work of the Section is oriented toward these goals. Two problems are studied. One problem involves the cardiovasular system and beta-adrenoceptors which i.a. regulate this system. Studies in that field suggest that compounds with multiple pharmacophores of the antagonist type can effectively block this system for periods an order of magnitude longer than those compounds with a single pharmacophore. This blockade can be shown both in vivo and ex vivo experiments. The joining of several antagonist pharmacophores into one molecule, on the other hand, does not result in the introduction of agonist activity, a change which was observed in the field of peptidic hormones. Another problem studied involves solubilizers for compounds of biomedical interest; from those steroids were studied. Subnormal serum levels of sex hormones is a typical problem of the elderly. Basic research on solubilizers performed in the Section has enabled the development of a practical oral dosage form of these hormones.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 AG 00047-14 LCMB

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Structure-Function Relationships in Hemoglobin and Erythrocytes

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
Joseph M. Rifkind, Research Chemist, Lab. of Cellular & Molecular Biology, NIA

Other:

| | | | | |
|---|---|---|---|---|
| P. Chuknyiski | Visiting Fellow | IBS | LCMB | NIA |
| A. Levy | Visiting Associate | IBS | LCMB | NIA |
| P.T. Manoharan | Visiting Scientist | IBS | LCMB | NIA |

COOPERATING UNITS *(if any)*
Johns Hopkins University, University of Alabama (G. Elgavish), Benedict College, South Carolina (K. Alston) and State University of New York at Buffalo (F. Davis)

LAB/BRANCH
Laboratory of Cellular and Molecular Biology

SECTION
Inorganic Biochemistry Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| | | |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to study the mechanisms involved in regulating the binding of oxygen to hemoglobin and the transport of oxygen to the tissues. The project also focuses on ways in which these functions are impaired and change with age. We have therefore studied the mechanisms involved in the oxidation of hemoglobin. Oxidation affects oxygen transport because it produces nonfunctional hemoglobin, which no longer binds oxygen. These studies have been extended to include an investigation of the stability of the entire erythrocyte and the erythrocyte membrane as well as other structure function relationships in membranes.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00048-10

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Ion Transport Mechanisms and Aging

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | |
|---|---|---|
| Jeffrey P. Froehlich | Medical Officer | LMA, GRC, NIA |
| Other: | | |
| Phillip F. Heller | Chemist | LMA, GRC, NIA |
| R.W. Albers | Chief, Neurochemistry Section | LNC, NINDCDS |
| A.S. Hobbs | Assistant Research Professor | Dept. Physiology Univ of Maryland |
| E.L. Lakatta | Chief, Cardiovascular Section | CPB, NIA |

COOPERATING UNITS *(if any)*
Laboratory of Neurochemistry, NINDCDS, NIH;
Cardiology Section, Clinical Physiology Branch, NIA;
Dept. Physiology, Univ. Maryland

LAB/BRANCH
Gerontology Research Center, Laboratory of Molecular Aging

SECTION
Biophysics and Intermediary Metabolism Sections

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, MD 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 1 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Previous manual mixing studies demonstrating decreased $Ca^{2+}$ uptake activity in cardiac muscle sarcoplasmic reticulum (SR) with age have been extended to include measurements of transport function carried out on a physiologic (millisecond) time scale. The results demonstrate linear rates of ATP-dependent transport activity that are ten times faster than those previously determined by manual filtration (time scale of seconds to minutes). Active $Ca^{2+}$ accumulation in SR isolated from old rat myocardium showed an average decline in activity of 43% compared to that found in SR prepared from young adult rat hearts ($p > .05$). These findings lend additional support to the hypothesis relating the prolonged relaxation time in senescent myocardium to a decline in SR $Ca^{2+}$ pump activity.

The kinetics of the phosphoenzyme transition $E_1P \rightarrow E_2P$ in the Na,K-ATPase reaction cycle were investigated. The results indicate that the transition is among the fastest reactions of the catalytic cycle and are consistent with a model in which de-occlusion of the transported ions are rate-limiting in the translocation sequence.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00051-04 LMA

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Phosphate and Calcium Homeostasis: Pathophysiology of Osteopenia in Aging

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | |
|---|---|---|
| Bertram Sacktor | Chief, Laboratory of Molecular Aging | LMA, GRC, NIA |
| C. Tony Liang | Research Chemist | LMA, GRC, NIA |
| Bernard A. Bulos | Research Chemist | LMA, GRC, NIA |
| Linda Cheng | Research Chemist | LMA, GRC, NIA |
| Charles Filburn | Research Chemist | LMA, GRC, NIA |
| Gary Kiebzak | Staff Fellow | LMA, GRC, NIA |
| Makoto Ishida | Visiting Associate | LMA, GRC, NIA |

COOPERATING UNITS *(if any)*

| | | |
|---|---|---|
| David Spector | Renal Division, Department of Medicine | JHU |
| Edward Kraus | Renal Division, Department of Medicine | JHU |

Renal Division, Department of Medicine, Johns Hopkins University, Baltimore, MD

LAB/BRANCH

Gerontology Research Center, Laboratory of Molecular Aging

SECTION

Intermediary Metabolism Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, MD 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 8.1 | 5.6 | 2.5 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*


This report describes studies on the mechanisms of phosphate and calcium homeostasis relevant to changes in mineral metabolism during the aging process. The findings relate to investigations on:

(a) Age-related phosphaturia and hypophosphatemia.

(b) Renal adaptation to phosphate load in the acutely thyroparathyroidectomized rat: rapid alteration in brush border membrane phosphate transport.

(c) Phosphate reabsorption in progressive renal failure: effects of parathyroidectomy and phosphate restriction.

(d) Phosphate uptake in cultured renal cells: mechanisms of hormonal regulation.

(e) The physiological mechanism by which 1,25-dihydroxycholecalciferol increases intestinal calcium absorption.

(f) The biochemical mechanisms by which 1,25-dihydroxycholecalciferol increases intestinal calcium absorption.

(g) Age-dependent changes in the metabolism of vitamin D.

(h) Regulation of intestinal calcium absorption by diet.

(i) Renal calcium transport, sodium/calcium exchange in renal tubule baso-lateral membranes and the action of parathyroid hormone.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00052-04 LMA

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Pathophysiological and Hormonal Regulation of Membrane Transport Systems.

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | |
|---|---|---|
| Bertram Sacktor | Chief, Laboratory of Molecular Aging | LMA,GRC,NIA |
| C. Filburn | Research Chemist | LMA,GRC,NIA |
| J. Kinsella | Staff Fellow | LMA,GRC,NIA |
| S. Guggino | Staff Fellow | LMA,GRC,NIA |
| J. Wehrle | Staff Fellow (EOD 1/84) | LMA,GRC,NIA |
| S. El-Seifi | Visiting Fellow (DOD 4/84) | LMA,GRC,NIA |

COOPERATING UNITS *(if any)* B. Suarez-Isla, Visiting Fellow, LN, GRC, NIA
M. Farquhar and D. Kerjaschki, Dept Cell Biol, Yale Univ of Med, New Haven, CT
D. Spector, Renal Div, Dept Med, JHU
G. Hill, Dept Pathol., and W. Guggino, Dept of Physiology, JHU

LAB/BRANCH
Gerontology Research Center, Laboratory of Molecular Aging

SECTION
Intermediary Metabolism Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, MD 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 6.5 | 5.0 | 1.5 |

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This report describes studies on the biochemical, biophysical, and physiological mechanisms of membrane transport in the kidney, the regulation of these transport systems by hormones and various pathophysiological effectors, and the changes which occur in renal function in aging. The findings relate to investigations on:

(a) Sodium-proton exchange activity, adaptation in metabolic acidosis and regulation by hormones.

(b) Titratable acid (phosphate) excretion in response to metabolic acidosis.

(c) Characterization of the sodium-protein exchange carrier.

(d) Cell culture systems for examining the mechanisms of hormonal regulation.

(e) Chronic renal insufficiency and the pathogenesis of progressive glomerular sclerosis in aging.

(f) Sodium-dependent transport of inorganic sulfate in renal brush border membranes.

(g) Renal transport in the diabetic (streptozotocin-treated) rat: transport of β-hydroxybutyrate in the ketotic animal.

(h) Identification and characterization of ion channels in epithelial cells: hormonal regulation.

(i) Phospholipid and calcium-dependent protein kinase (Protein kinase C).

(j) Distinctive microdomains in the kidney proximal tubule brush border membrane.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG00062-11 LBS

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Daydreaming and Aging: Normative and Experimental

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: L.M. Giambra Senior Investigator LBS, GRC, NIA

COOPERATING UNITS *(if any)*

None

LAB/BRANCH
Laboratory of Behavioral Sciences

SECTION
Learning and Problem Solving Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, MD 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| .8 | .5 | .3 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this work is to determine the parameters of task-unrelated-thought-intrusions (TUTIs) both spontaneous (daydreams) and otherwise, as well as related mental activity such as insight, intuition, and mindwandering. An additional purpose is to investigate the relation between sustained attention and age. The purposes are accomplished through the use of retrospective questionnaires and by controlled laboratory manipulation. Outcomes derived from these purposes and obtained over this fiscal year were: (a) Three samples of men and women tested in 1962-64 and 1980-84 who ranged in age from 20 to 94 years and who performed the Mackworth Clock sustained vigilance task, were observed to show no statistically significant age differences in level of performance as measured by the percentage of targets detected, and by the mean response time for detected targets; this outcome represents one of the few that has failed to observe such performance differences when the full adult lifespan was sampled and strongly suggests an unchanged sustained attentional capacity for different age cohorts. (b) Four studies which varied the nature of the vigilance task and the method of determining TUTIs were carried out on men and women from 17 to 94 years of age. Three of these studies obtained an inverse relationship between the frequency of the TUTIs and the age of the participants. This finding was a laboratory corroboration of a previous finding which found an inverse relation between daydreaming frequency, as determined from a retrospective questionnaire, and age represented by the adult lifespan. These findings are interpreted in terms of reduced potency with increasing age of a thought-generating mechanism within the nonconscious mind.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00063-17 LBS

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Learned Modification of Visceral Function in Animals

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | |
|---|---|---|
| Bernard T. Engel, Ph.D. | Chief, LBS | LBS, GRC, NIA |
| Mark Talan, M.D. | Visiting Associate | LBS, GRC, NIA |
| Gyorgy Bardos, Ph.D. | Visiting Associate | LBS, GRC, NIA |

COOPERATING UNITS *(if any)*

Laboratory of Cellular and Molecular Biology

LAB/BRANCH

Laboratory of Behavioral Sciences

SECTION

Psychophysiology

INSTITUTE AND LOCATION

National Institute on Aging, National Institutes of Health, Baltimore, MD 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 6.2 | 2.5 | 3.7 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to investigate the role of the central nervous system in behavior. In some experiments monkeys (Macaca mulatta) are used to examine the extent to which the cardiovascular system can be modified by instrumental conditioning. In other experiments we examined age-related thermoregulatory changes in mice.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00064-23 LBS

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Problem Solving and Aging

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*


| | | | |
|---|---|---|---|
| PI: | D. Arenberg | Section Chief | LBS, NIA |
| Others: | L.M. Giambra | Senior Investigator | LBS, NIA |
| | J.D. Sinnott | Towson State University | |


COOPERATING UNITS *(if any)*

Francis Scott Key Medical Center

LAB/BRANCH

Laboratory of Behavioral Sciences

SECTION

Learning and Problem Solving Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, MD 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.7 | .9 | 1.8 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*


Among the goals of this project are to describe age differences and changes in reasoning performance and to investigate psychological processes underlying such age-related performance. In a major longitudinal study of logical problem solving in men, cross-sectional age differences and changes over six years were found in both analysis, i.e., obtaining information, and synthesis, i.e., using information to reach a solution.

In the study of individual models of complex concept learning problems, two of the models were validated using problems other than those on which the models were constructed. Each individual's model is micro-theory detailing the memory, inference, and decision processes, and the capacities of the memory stores used in solving the problems. A micro-theory is constructed from eight problems during which the problem solver thinks aloud throughout each problem. Two models, one for an 18 year old man and the other for a 63 year old man, were successfully validated using several criterion measures of how well each model predicted the solution behavior on eight other problems. The processes identified in the two models were similar except for an additional mechanism in the model of the older man which attempts to compensate for his more limited memory capacity by representing the stored information more efficiently, thus reducing the cognitive strain of the task.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00065-24 LBS

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Verbal Learning and Age

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*


PI: D. Arenberg Section Chief LBS, NIA

Others: E. A. Robertson-Tchabo University of MD, College Park
J. D. Sinnott Towson State University


COOPERATING UNITS *(if any)*

Francis Scott Key Medical Center

LAB/BRANCH

Laboratory of Behavioral Sciences

SECTION

Learning and Problem Solving Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, MD 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.4 | .4 | 2.0 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*


Among the goals of this project are to describe adult age differences and changes in memory and learning performance and to investigate psychological processes underlying such age-related performance. This year, four memory measures were analyzed together with response-time measures to compare the age correlations for men and women and to determine the degree to which these correlations with memory were attributable to rate of information processing. The age correlations were similar in magnitude for men and women; and very little of these correlations were attributable to measures of information processing rate.

DEPARTMENT OF HEALTH AND HUMAN SERVICES · PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 AG 00066-23 LBS

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Perceptual Retention and Age

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: D. Arenberg Section Chief LBS, NIA

COOPERATING UNITS *(if any)*

Francis Scott Key Medical Center

LAB/BRANCH

Laboratory of Behavioral Sciences

SECTION

Learning and Problem Solving

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, MD 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| .7 | .1 | .6 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Among the goals of this project is to describe adult age differences and changes in nonverbal memory performance. This year, cross-sectional data from the Benton Visual Retention Test were analyzed for 365 women participating in the Baltimore Longitudinal Study of Aging (BLSA). The correlation was -.50 which is quite similar to correlations previously reported for men in the BLSA. The pattern of ten-year age-group means was also similar to that of men; age differences were small for the youngest groups and largest late in life.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00067-17 LBS

PERIOD COVERED

October 1, 1983 through September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Learned Modification of Visceral Function in Man

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | |
|---|---|---|
| Bernard T. Engel, Ph.D. | Chief, LBS | LBS, GRC, NIA |
| Kathleen A. McCormick, Ph.D. | Research Nurse | LBS, GRC, NIA |
| Kathryn L. Burgio, Ph.D. | Staff Fellow | LBS, GRC, NIA |
| Michael Glasgow, Ph.D. | Research Physiologist | LBS, GRC, NIA |

COOPERATING UNITS *(if any)*

Care First Medical Clinic, Francis Scott Key Medical Center, Johns Hopkins University School of Medicine

LAB/BRANCH

Laboratory of Behavioral Sciences

SECTION

Psychophysiology

INSTITUTE AND LOCATION

National Institute on Aging, National Institutes of Health, Baltimore, MD 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 6.9 | 3.1 | 3.8 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is concerned with the application of behavioral methods and principles to clinical medicine. Subjects are patients selected from various medical clinics, or normal subjects who are studied to evaluate potential clinical methods. The main focus of this project is on clinical problems especially relevant to middle aged or elderly persons.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00075-06 LBS

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Stress, Coping, and Personality in Aging Men and Women

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Paul T. Costa, Jr., Ph.D., Chief, Stress & Coping Section, LBS, GRC, NIA

COOPERATING UNITS *(if any)*

Psychophysiology Section, LBS
Epidemiology and Demography and Biometry Program
Dept. of Psychiatry, Duke University Medical School

LAB/BRANCH

Laboratory of Behavioral Sciences

SECTION

Stress & Coping Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, MD 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 4.5 | 2.5 | 2.0 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is concerned with the effects of stressors, coping mechanisms, and enduring personality dispositions on psychological and health outcomes. One study examines the impact of changes in marital-status, residence, occupation and employment status over a 10-yr. follow-up period in a national probability sample of over 14,000 individuals initially aged 25-74, on perceptions of health, general well-being, personality, morbidity and mortality; a second tests the hypothesis that individuals with different personality traits adapt differently to a common stressor; a third study identified two additional domains of personality--agreeableness and conscientiousness--which were confirmed in both self-reports of personality and peer ratings; a fourth study examines the relations between agreeableness and conscientiousness and assessments of the coronary prone behavior pattern (Type A) among individuals undergoing coronary angiography; a fifth examined the longitudinal course of social support and found little change over 6 and 12-yr. intervals and substantial stability in individual scores; a sixth study on patients undergoing coronary angiography demonstrated that patients' neuroticism scores were unrelated to extent of coronary stenosis but were related to atypical features in reports of their chest pain episodes. The seventh study investigating the factorial and conceptual dimensions of the Illness Behavior Questionnaire (IBQ) utilizing over 1,000 subjects from various health-care- and non-health-care seeking groups failed to replicate the hypothesized number of factors and led to reinterpretations of several of the factors.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00076-05 LBS

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Openness to Experience and Coping Styles

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Robert R. McCrae, Research Psychologist, Stress & Coping, LBS, GRC, NIA

Paul T. Costa, Jr., Chief, Stress & Coping, LBS, GRC, NIA

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Behavioral Sciences

SECTION

Stress & Coping Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, MD 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.3 | .6 | .7 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is concerned with the personality disposition of openness to experience and its relation to coping styles. One study investigates the correspondence between openness and dimensions of personality found in analyses of English-language trait names. One major system of personality is based on the assumption that important individual difference variables will have been encoded in natural languages, and analyses of English have repeatedly shown five factors. To determine correspondences between openness and these five dimensions, an adjective checklist was given to 498 men and women, aged 24 to 89, on whom measures of openness were available. Results showed that the five factors could be recovered in this sample and that one factor, previously called "culture", corresponded to openness to experience. Correlations of .52 between this factor and spouse ratings of openness obtained three years earlier gave strong evidence of the match across time, observer, and instrument. A second study assessed the effectiveness of a wide range of coping mechanisms. Frequency of reported use, perceived utility in solving the problem, perceived helpfulness in reducing distress, and relation to subsequent measures of well-being were all used as criteria of effectiveness. Analyses showed that rational action, seeking help, faith, and humor were generally effective; whereas hostile reactions, indecisiveness, self-blame and wishful thinking were least effective. Both humor, a coping mechanism associated with openness, and faith, a mechanism associated with closedness, were among the more effective mechanisms, suggesting that individual differences in openness to experience lead to different but equally effective ways of coping.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00077-02 LBS

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Studies of the Oral Physiological Status of Man During Aging

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Marc W. Heft Senior Staff Fellow, Stress & Coping, LBS, GRC, NIA

COOPERATING UNITS *(if any)*

NIDR, NIH

LAB/BRANCH

Laboratory of Behavioral Sciences

SECTION

Stress & Coping

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, MD 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.5 | 0.5 | 0.0 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

There has been little systematic investigation of tissues within the aging oral cavity. The purpose of this project is to assess the oral physiological status of participants in the Baltimore Longitudinal Study and thus provide baseline information which is lacking.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01-AG-00093-12-CPB

PERIOD COVERED: October 1, 1983 to September 30, 1984

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)
Cellular Basis of Regulation of the Humoral Immune Response

PRINCIPAL INVESTIGATOR (List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)

| | | | |
|---|---|---|---|
| PI: | A. A. Nordin | Research Chemist | CPB, NIA |
| Others: | J. J. Proust | Visiting Associate | CPB, NIA, EOD 10/3/83 |
| | G. O. Collins | Biologist | CPB, NIA |
| | M. A. Buchholz | Bio. Lab Tech | CPB, NIA |

COOPERATING UNITS (if any)
None

LAB/BRANCH
Gerontology Research Center, Clinical Physiology Branch

SECTION
Clinical Immunology Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 4.4 | 2.2 | 2.2 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

The role of soluble factors produced by lymphocytes and monocytes in controlling the activation, proliferation and differentiation of lymphocytes participating in immunological functions was studied. Studies were performed with B and T lymphocytes to establish the requirement of various soluble factors (interleukins) for the induction of immunoglobulin synthesis and the development of cytotoxic lymphocytes.

B-cells. Supernatants derived from a cloned murine T-cell hybridoma line induced the proliferation and differentiation of purified B-cells stimulated with soluble anti μ. Column chromatography of the supernatant distinguished these two activities based on M.W. The larger M.W. material induced proliferation but no Ig synthesis while the smaller M.W. material induced both activities. Subsequent studies showed that this "interleukin-like" activity was due solely to Mycoplasma hyorhinis contamination of the T-cell hybridoma and was not a function of the hybridoma cells.

T-cells. The activation of resting T-cells to cytotoxic lymphocytes (CTL) by lectins or alloantigens is dependent on the presence of interleukins. The induction of CTL by the lectin, leukogglutinin, is dependent on the presence of only interleukin-2 (IL-2). Alloantigen induction of CTL is also dependent on IL-2 but requires in addition other soluble factors contained in supernatants derived from simulated El-4 cells.

The significance of these studies is that soluble factors play an ever increasing critical role in regulating lymphocyte activity. Characterization of these pharmacologically active substances and their role(s) in establishing immune function are important aspects in the understanding of the immune system.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01-AG-00095-11-CPB

PERIOD COVERED
October 1, 1983 - September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
The Role of Cell Membrane Structures on Cellular Recognition

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | W. H. Adler | Medical Officer, PHS | CPB, NIA |
| Others: | J. E. Nagel | Medical Officer, PHS | CPB, NIA |
| | R. K. Saxena | Visiting Associate | CPB, NIA left 2/84 |
| | Q. B. Saxena | Visiting Associate | CPB, NIA left 2/84 |

COOPERATING UNITS *(if any)*
Dr. Richard Winchurch, Department of Surgery, Johns Hopkins University, Francis Scott Key Medical Center, 4940 Eastern Avenue, Baltimore, MD 21224

LAB/BRANCH
Gerontology Research Center, Clinical Physiology Branch

SECTION
Clinical Immunology Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.2 | 1.8 | .4 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Continuing the research on control mechanisms in immune function has demonstrated that spleen cells from old mice produce more interferon than do cells from young mice, but the cells from the old mice are less affected by the interferon because of a relative lack of membrane interferon receptors. Therefore interferon and interferon inducing agents have a greater effect on the cells from young mice. Also, the metal Zinc has been shown to be able to boost in vitro antibody responses of spleen cells from old mice. Along with other evidence that Zinc is important in the activation of thymic hormone from an inactive to the active state it may be that in vivo administration of Zinc to old mice or humans could improve immune function.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01-AG-00096-11-CPB

PERIOD COVERED: October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*: Low Temperature Effects on Cells of Aging Individuals

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*


| | | | |
|---|---|---|---|
| PI: | M. A. Brock | Research Biologist | CPB,NIA |
| Others: | W. H. Adler | Medical Officer, PHS | CPB,NIA |


COOPERATING UNITS *(if any)*: None

LAB/BRANCH: Gerontology Research Center, Clinical Physiology Branch

SECTION: Clinical Immunology Section

INSTITUTE AND LOCATION: NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.2 | 1.1 | .1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*


Splenic lymphocytes from young, 15 month old and 24 month old C57BL/6 mice housed in a constant environment were studied. Single cell suspensions, both unfrozen and cryopreserved, were cultured in vitro with the T cell mitogens, phytohaemagglutinin and Concanavalin A, and the B cell mitogen, lipopolysaccharide. Functional capacity of the T and B lymphocytes was assessed by the mitogen-induced incorporation of tritiated thymidine by dividing cells.

Seasonal rhythmicity in the incorporation of tritiated thymidine was exhibited by splenic lymphocytes from mice of three different ages. The responses to both T-cell mitogens exhibited marked decreases in amplitude and increase in freerunning periods with age. Activated B-cells exhibited little change in amplitude but markedly longer freerunning periods. In comparing the three age groups, the rhythms were not in synchrony with each other, and those of the older mice were not in synchrony with the calendar year.

The "variability" and lack of age-related declines in lymphocytic responses to mitogens previously reported by others may be due to grouping data for all seasons and to testing during phases of the circannual rhythm characterized by similar responses of all age groups.

Cryopreservation of lymphocytes from older mice resulted in lower recoveries of viable and functional cells as compared to cryopreserved lymphocytes from young mice. Seasonal rhythmicities in the recoveries of young mouse cells also were exhibited and paralleled those of unfrozen cells.

The significance of these results is 1) their support of the hypothesis that decay of circadian and circannual organization may be involved in physiological deterioration with age, and 2) cryopreservation stress confers selective injury, probably involving the plasma membrane, to lymphocytes from older mice.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01-AG-00101-08-OSD

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Relation between Nutritional State and Aging

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
*(Name, title, laboratory, and institute affiliation)*

Charles H. Barrows, Jr., SCN, OSD, NIA

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

Gerontology Research Center, Office of the Scientific Director

SECTION

Section on Comparative Nutrition

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.0 | 2.0 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A direct linear relationship was established between hepatic cell volume, based on DNA, and cellular protein and enzymatic activities. In control animals age results in small cells and therefore less protein and enzymatic activities per cell size. Dietary manipulation minimizes these age effects but also results in small cells in all age groups. In addition it was found that the biochemical characteristics of animals depend upon the dietary manipulations to which they are exposed. In order to determine whether the development of specific diseases may be influenced differentially by dietary manipulations genetically determined diabetic mice were studied. With approximately 40% mortality in the diabetic animals fed 24% protein ad libitum, those fed ad libitum a 24% protein diet diluted 50% with cellulose experienced 100% mortality; the intermittent fed animals, 30% mortality; while the low protein (4%) ad libitum fed animals, had no mortality. In addition, observations indicate that all of the 24% protein ad libitum fed animals have polyuria while there is considerably less polyuria in the intermittent animals and thus far no polyuria in the 4% protein ad libitum fed animals. Thus these preliminary findings indicate beneficial effects due to dietary manipulation especially among animals fed the low protein diet which contains approximately 50% more sucrose than the 24% protein diet.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01-AG-00104-08-CPB

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Clinical Immune Survey of the Longitudinal Project Participants

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | W. H. Adler | Medical Officer | CPB, NIA |
| Others: | A. A. Nordin | Research Chemist | CPB, NIA |
| | J. E. Nagel | Medical Officer | CPB, NIA |
| | B. S. Bender | Medical Staff Fellow | CPB, NIA |
| | F. J. Chrest | Biologist | CPB, NIA |
| | R. S. Pyle | Bio. Lab Tech. | CPB, NIA |
| | B. A. Dorsey | Bio. Lab Tech. | CPB, NIA |

COOPERATING UNITS *(if any)*
None

LAB/BRANCH
Gerontology Research Center, Clinical Physiology Branch

SECTION
Clinical Immunology Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 4.2 | 1.9 | 2.3 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The immune function of participants in the Baltimore Longitudinal Study of Aging is evaluated to determine age-associated changes and the possible effects of these changes on the incidence and type of disease. Another major goal is to evaluate the ability of existing assays of immune function to provide an accurate assessment of the level of immune competence of aging individuals and to refine and develop new methods and assays to evaluate host defense mechanisms.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00113-1 LCMB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

In vivo NMR Studies of Aging in Cells and Animals

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | | | |
|---|---|---|---|---|---|
| PI: | Gunther L. Eichhorn | Chief, LCMB | IBS | LCMB | NIA |
| Others: | Rajasekharan P. Pillai | Visiting Associate | IBS | LCMB | NIA |
| | Daniel Waysbort* | Visiting Associate | IBS | LCMB | NIA |

*On leave from Israel Institute for Biological Research, Ness-Ziona

COOPERATING UNITS *(if any)*

Department of Nuclear Medicine, Johns Hopkins University (Drs. Glicksen & Wagner);
Department of Radiological Chemistry, Johns Hopkins University (Dr. Kan);
Department of Radiology, Francis Scott Key Medical Center (Dr. Goldman)

LAB/BRANCH

Laboratory of Cellular and Molecular Biology

SECTION

Inorganic Biochemistry Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.5 | 1.4 | 0.1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

NMR is used for the non-invasive study of aging in cells and animals. Probes designed for use with a narrow bore Varian XL-200 spectrometer are employed to perfuse cells such as human fibroblasts of varying passage and from donors of differing ages. The cells are then studied by NMR with $^{31}P$ and other atomic nuclei to determine age changes in metabolism. The cells are challenged by various metabolites and drugs to determine age changes in the effects of these substances on the cells.

A Biospec NMR spectrometer (310/1.9) is used to study age changes in animals metabolism by similar techniques, and the metabolic changes are compared to morphological by NMR imaging techniques, which are also useful for studying changes in the distribution of drugs and metabolites.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00120-07 LN

PERIOD COVERED: October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Blood-Brain Barrier and Central Nervous System Function

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| S.I. Rapoport | Chief | LN | NIA |
| P.J. Robinson | Visiting Associate | LN | NIA |
| N.H. Greig | Visiting Fellow | LN | NIA |

COOPERATING UNITS *(if any)*

Laboratory of Neuropathology and Neuroanatomical Studies, NI, NCDS
Department of Opthalmology, University of Pennsylvania
Department of Chemistry, Johns Hopkins University

LAB/BRANCH

Laboratory of Neurosciences

SECTION

Cerebral Physiology and Metabolism

INSTITUTE AND LOCATION

NIA, NIH, Bethesda, MD 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3.75 | 2.75 | 1.0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Brain uptake of intravenously injected 14C-morphine was shown in rats to be related to arterial pH, and to be augmented by alkalosis. The results are consistent with an increased analgesic effect of morphine during alkalosis in man. In rats, acidosis increased penetration of intravascular sodium fluorescein into the eye, at the retinal pigment epithelium. Both morphine and fluorescein effects are consistent with the pH-partition hypothesis for drug entry into the nervous system.

Brain uptake of the water soluble anti-cancer drug Melphalan is very low, because the cerebrovascular-permeability area product is close to that of sucrose. A theoretical model relating glucose transport into the brain and brain glucose utilization was developed and applied to hypoglycemic states. Dimethyl sulfoxide, reported to open the blood-brain barrier, was not effective in mice and rats.

Osmotic opening of the blood-brain barrier was used in humans to allow anti-neoplastic agents into the brain for treating brain tumors. The blood-brain barrier in rats, following osmotic treatment, recovered more rapidly to larger than to smaller intravascular molecules, suggesting that barrier opening is mediated by a pore mechanism. Osmotic treatment increased the permeability of interendothelial tight junctions to intravascular lanthanum. The rate of loss of methotrexate from the brain, following loading in association with osmotic blood-brain barrier opening, was slower than that of sucrose, suggesting cell uptake of the anticancer drug.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00121-07 LN

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Function of Peripheral Nerve and Muscle

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| C. Latker | Sr. Staff Fellow | LN | NIA |
| E. Rechthand | Med. Staff Fellow | LN | NIA |
| A. Weerasuriya | Visiting Associate | LN | NIA |

COOPERATING UNITS *(if any)*
Experimental Morphology Section, NIA; Department of Medical Engineering, University of Linkoping, Sweden, Department of Biophysics, SUNY, Buffalo; Laboratory of Biophysics, NINCDS.

LAB/BRANCH
Laboratory of Neurosciences

SECTION
Cerebral Physiology and Metabolism

INSTITUTE AND LOCATION
LN, NIA, NIH, Bethesda, Maryland 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 4.75 | 4.75 | 0 |

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Blood-vessels of nerve are comparable to those of the central nervous system, and are lined by a continuous endothelium with intercellular tight junctions. They form part of the blood-nerve barrier, together with the perineurium. The electrical properties of the perineurium were examined by AC impedance techniques, which demonstrated that the perineurium has a high resistance to ion flow and electrical polarization characteristics of intercellular tight junctions.

Hypertension, induced by vascular perfusion of the nerve damages the vascular endothelium by forming submembrane blisters, and increases permeability to intravascular tracers, horseradish peroxidase and microperoxidase. Alkaline phosphatase, an enzyme characteristic of epithelia involved in transport, is found in blood vessels of the rat but not of the frog endoneurium, and in the perineurium of the frog nerve but not of the rat nerve, suggesting differential transport properties of the tissues in relation to species. Low permeabilities of capillaries of the frog sciatic nerve suggest that ions cross the capillaries by the paracellular route, and are not transported actively across the vascular endothelium. Similarly, calcium appears to traverse the frog perineurium by a passive diffusion. Capillaries of the frog sciatic nerve demonstrate increased permeability following nerve transection and after 1 week of Wallerian degeneration. Endoneurial capillary integrity therefore depends on the integrity of the nerve itself.

An adequate blood supply to the nerve is required to maintain nerve function and integrity. Blood flow in the rat sciatic nerve was measured with a laser Doppler flowmeter and radiotracer techniques, and was shown to be close to that found for white matter of the brain. During systemic hypotension, there does not appear to be autoregulation of flow, as flow falls in proportion to systemic blood pressure.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00122-07 LN

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Pharmacology of Central and Peripheral Catecholaminergic Nervous Systems

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

A. Hervonen Visiting Scientist LN NIA

COOPERATING UNITS *(if any)*

Section of Gerontology, Departments
of Biomedical Sciences and Public Health
University of Tampere, Finland

LAB/BRANCH
Laboratory of Neurosciences

SECTION
Cerebral Physiology and Metabolism

INSTITUTE AND LOCATION
NIA, NIH, Bethesda, MD 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.5 | 1.5 | 0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Age changes were demonstrated in the human stellate ganglion, a sympathetic ganglion. These included a loss of cytoplasmic catecholamine fluorescence, dendritic hypertrophy and neuroaxonal dystrophy. In adult paravertebral human sympathetic ganglia, immunoreactivity to the following peptides [Met$^5$]enkephalin, [Met$^5$]enkephalin-Arg$^6$-Phe$^7$ and bombesin-gastrin releasing peptide, as well as Substance P, was localized in varicose nerve fibers, but not in cell bodies.

Increased secretion by autonomic paraganglia is thought to contribute to elevated plasma catecholamines levels in senescent Fischer-344 rats. In such paraganglia, there was a progressive increase, by up to 10 fold, in the number of cells between 3 and 24 months of age, and in tyrosine hydroxylase and choline acetyltransferase activities, enzymes necessary for synthesis of catecholamines and acetylcholine, respectively. Adrenalectomy did not affect choline acetyltransferase but reduced tyrosine hydroxylase activity by 60% in senescent rats.

Age changes in cell number and catecholamine fluorescence of paraganglia suggested an active endocrine, secretory function in the older Fischer-344 rats. The catecholamine synthesizing enzymes, tyrosine hydroxylase, dopamine-$\beta$-hydroxylase and phenylethanolamine N-methyltransferase were demonstrated by immunohistochemical techniques.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00123-06 LN

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Synapse Development, Specificity and Mechanism In Culture

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| B.A. Suarez-Isla | Visiting Fellow | LN | NIA |
| J.W. Cosgrove | Senior Staff Fellow | LN | NIA |
| B. Horwitz | Senior Staff Fellow | LN | NIA |

COOPERATING UNITS *(if any)*
Salk Institute, LaJolla, CA
Department of Neurobiology, University of Illinois

LAB/BRANCH
Laboratory of Neurosciences

SECTION
Cerebral Physiology and Metabolism

INSTITUTE AND LOCATION
NIA, NIH, Bethesda, MD 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3.0 | 2.5 | .5 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Synapse formation, synapse stabilization and neurotrophic effects on ionic channels were studied using neurons and muscle cells in culture. Synapses were detected and investigated by electrophysiological recording. Single ionic conductances were studied with the extracellular patch clamp technique on cultured muscle cells or on bilayers formed at the tip of patch pipets. Neurons from chick spinal cord form stable synapses with muscle cells in culture, eliciting changes in the muscle cell membrane that resemble maturation in vivo. Stabilization of synapses leads to increased aggregation of muscle acetylcholine receptors, blocking of a Ca2+-dependent K+-conductance and increased tetrodotoxin sensitivity of the action potential mechanism. Blocking of the Ca2+-dependent K+-conductance can be elicited in the absence of innervation after treatment of muscle cells with a low molecular weight fraction (< 4,000 D) obtained from chick spinal cord conditioned medium or with a spinal cord extract.

Calcium channel blockers impair the ability of dissociated neurons to form synapses, and inhibit neurite extension. The degree of inhibition depends on the age in ovo and is more marked in neurons dissociated from older embryos. Synapse formation is also impaired by purified monoclonal antibodies directed against the acetylcholine receptor in muscle cells. A mechanism by which a change in electrical activity at a synapse results in a local structural change was proposed; and was used to show how competition between neighboring afferent inputs leads to selective synaptic stabilization, and to suggest a role for dendritic spines in reducing this competition.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00125-06 LN

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 charecters or less Title must fit on one line between the borders.)*

Cerebral Metabolism, Relation to Brain Function and Aging

PRINCIPAL INVESTIGATOR *(List other professionel personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| T. Soncrant | Staff Fellow | LN | NIA |
| G. Pizzolato | Visiting Fellow | LN | NIA |

COOPERATING UNITS *(if any)*

Department of Neuropathology
University of Western Ontario

LAB/BRANCH

Laboratory of Neurosciences

SECTION

Cerebral Physiology and Metabolism

INSTITUTE AND LOCATION

NIA, NIH, Bethesda, MD 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 6.7 | 4.1 | 2.6 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The regional cerebral metabolic rate for glucose ($rCMR_{glc}$) was examined in Fischer-344 rats and beagle dogs in relation to age and pharmacological stimulation. In beagles, older than 6 yr, many brain regions showed reduced $rCMR_{glc}$ particularly those involved with sensory function. The brains of the beagles showed no evidence of senile plaques or of neurofibrillary tangles, which characterize Alzheimer's disease in man, nor significant losses of neurons.

Oxotremorine, a cholinergic agonist, stimulated $rCMR_{glc}$ in awake rats in brain regions associated with memory function, further supporting a role for acetylcholine in memory. Arecoline, another cholinergic agonist, also stimulated $rCMR_{glc}$ in a number of brain regions, including those with muscarinic receptors. The metabolic responses to arecoline were reduced in senescent as compared to younger rats, suggesting that, there is a defect in cholinergic function in the senescent rat brain. Metabolic responses in awake animals were not influenced by mild immobilization stress.

Dopaminergic function in the rat brain was examined by measuring $rCMR_{glc}$ in response to haloperidol (a dopaminergic antagonist), bromocriptine (an agonist) and sulpiride (a specific antagonist). At low drug doses, the responses occurred at dopaminergic receptor sites, whereas at higher doses generalized metabolic involvement occurred. The response to haloperidol was reduced in senescent as compared to younger Fischer-344 rats, despite the fact that higher concentrations of haloperidol accumulated within brains of old rats, suggesting a difference between old and young rats in central dopaminergic function. The metabolic responses to haloperidol were time-dependent and, with long-term treatment, demonstrated tolerance.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 AG 00126-05 LN

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Brain Function in Aging and Dementia

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| G. Berg | Medical Staff Fellow | LN | NIA |
| R. Duara | Medical Staff Fellow | LN | NIA |
| C.L. Grady | Psychologist | LN | NIA |
| N.L. Schlageter | Medical Staff Fellow | LN | NIA |

COOPERATING UNITS *(if any)* Laboratory of Clinical Sciences, NIMH
Nuclear Medicine Department, Clinical Center, NIH
University of Lund, Department of Clinical Neurophysiology, Lund, Sweden
Laboratory of Cerebral Metabolism, NIMH

LAB/BRANCH

Laboratory of Neurosciences

SECTION

Brain Aging and Dementia

INSTITUTE AND LOCATION

NIA, NIH, Bethesda, Maryland 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 7.5 | 5.4 | 2.1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The regional cerebral metabolic rate for glucose (rCMRglc) was examined, as a measure of cerebral functional activity in 21 healthy men between the ages of 21 and 83 years. rCMRglc was determined by means of positron emission tomography (PET) with 18-F-2-deoxy-D-glucose, under resting conditions, when the subject's eyes were covered and his ears plugged to reduce sensory input. Average hemispheric glucose utilization and glucose utilization in individual regions of the right and left hemispheres, did not decline significantly with age ($p > 0.05$). The study was extended and confirmed by examining brain metabolism in 40 healthy men in relation to age.

In young adult subjects with Down syndrome (19-27 yr.), rCMRglc was elevated by 20-40% as compared with age-matched healthy controls, indicating that brains of young adult Down syndrome subjects use glucose excessively despite retardation. In older adults with Down syndrome(> 35 yr.), rCMRglc was reduced as compared to its value in younger patients, associated with a decline in cognitive function suggestive of dementia. Similarly, adult patients with autism, an irreversible psychiatric disorder with onset in infancy and with a suspected neurological basis, showed elevated values of rCMRglc, to values between those in normal and Down syndrome subjects.

Adult patients with Alzheimer's disease showed variable reductions in rCMRglc, depending on the cognitive deficits. In mild-moderate Alzheimer's disease, relative rCMRglc was reduced in the parietal lobe as compared to other lobes. In severe Alzheimer's disease, rCMRglc was reduced throughout the cerebral hemispheres. The reductions were correlated with cognitive deficits, as determined by neuropsychological testing.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00127-04 LN

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Assessment of Neurochemical Markers in Relation to Age, Behavior and Dementia

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*


J.W. Ferkany Senior Staff Fellow

M. Bitar Staff Fellow


COOPERATING UNITS *(if any)*

Laboratory of Behavioral Sciences, NIA

LAB/BRANCH

Laboratory of Neurosciences

SECTION

Cerebral Physiology and Metabolism

INSTITUTE AND LOCATION

NIA, NIH, Bethesda, MD 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.5 | 2.5 | 0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standerd unreduced type. Do not exceed the space provided.)*


Age and strain differences in the activities of the neurotransmitter synthetic enzymes, choline acetyltransferase, glutamic acid decarboxylase and tyrosine hydroxylase were demonstrated in two strains of mice, A/J and C57BL/6J, between 4, 18 and 24 months. Age changes in neurochemical profiles therefore vary with genetic strain.

Striatal slices from the rat brain are less able to release acetylcholine in response to apomorphine, if they are derived from senescent as compared to young mature rats. The reduced ability corresponds to reduced motor behavior in older rats.

Binding of receptors for excitory amino acid neurotransmitters in the rat brain was evaluated in relation to treatment with the modulator, phenylalanyl-L-glutamate. This modulator increased the number of binding sites, to a greater extent in the striatum of brains of 34-month old rats than of 3-month old mature rats.

Rats made diabetic by administration of streptozotocin showed decreases in the activity of tyrosine hydroxylase, and increased concentrations of norepinephrine, in various brain regions, including the thalamus and hypothalamus. These results suggest that diabetes can alter brain monoamine metabolism and behavior subserved by monoamine neurotransmitters.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00128-04 LN

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Drug Pharmacokinetics, Relation to Pharmacodynamics and Senescence

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| S.I. Rapoport | Chief | LN | NIA |
| P. Robinson | Visiting Associate | LN | NIA |
| J.M. Schreiber | Chemist | LN | NIA |

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Neurosciences

SECTION

Cerebral Physiology and Metabolism

INSTITUTE AND LOCATION

NIA, NIH, Bethesda, MD 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 1 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A new analytical assay was developed, using gas liquid chromatography with nitrogen phosphorus detection, for the cholinergic agonist arecoline (1, 2, 5, 6-tetrahydro-1-methyl-3-pyridinecarboxylic acid methyl ester). The assay was applied to plasma and tissue samples of animals and to plasma samples of humans.

A model was developed for interpretation of the role of drug binding to plasma proteins in determining brain uptake of highly-bound drugs. The model took into account cerebral blood flow and the kinetics of protein binding.

A critical review of the issues of pharmacokinetics and pharmacodynamics of centrally acting drugs as they pertain to the elderly was published.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 AG00129-04 LN

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Transport Systems at the Blood-Brain Barrier

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Q.R. Smith Senior Staff Fellow LN NIA

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Neurosciences

SECTION
Cerebral Physiology and Metabolism

INSTITUTE AND LOCATION
NIA, NIH, Bethesda, MD 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3.0 | 3.0 | 0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Transport mechanisms at the blood-brain barrier were studied in the rat. An in situ brain perfusion technique was developed to examine carrier-mediated transport at the cerebral capillary endothelium. Brain perfusion with physiological saline solution or with blood did not alter cerebrovascular permeability to sucrose. Barrier permeability to nonelectrolytes was related linearly to lipid solubility. Large neutral amino acids cross the blood-brain barrier by facilitated diffusion. Cerebrovascular transport of large neutral amino acids did not change significantly in the Fischer-344 rat between 3 and 24 months of age. The cerebrovascular permeability to inorganic ions was low, comparable to permeability of a cell membrane, and followed the sequence K > Mg > Na > Cl > Ca. Chloride transport across the blood brain barrier was by a saturable system which was inhibited by monovalent anions. In contrast, calcium influx into the brain was directly proportional to the plasma concentration of ionized calcium. The low permeability of the cerebrovascular endothelium to Na was maintained with age in the rat, whereas the cerebrospinal fluid transfer constant for Na fell by 18%.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00130-02 LN

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less Title must fit on one line between the borders.)*
Neuropsychological Parameters in Aging and Dementia

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| J.V. Haxby | Staff Fellow | LN | NIA |
| C.L. Grady | Psychologist | LN | NIA |

COOPERATING UNITS *(if any)*
Rehabilitation Medicine Department, Clinical Center

LAB/BRANCH
Laboratory of Neurosciences

SECTION
Brain Aging and Dementia

INSTITUTE AND LOCATION
LN, NIA, NIH, Bethesda, Maryland 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 4.6 | 1.5 | 3.1 |

CHECK APPROPRIATE BOX(ES)
- [X] (a) Human subjects
  - [ ] (a1) Minors
  - [ ] (a2) Interviews
- [ ] (b) Human tissues
- [ ] (c) Neither

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Neuropsychologically relevant mental abilities are studied in healthy men at different ages, in patients with clinically-diagnosed Alzheimer's disease, and in adults with Down syndrome at different ages. Tests are administered to evaluate intelligence, memory, language, visual attention, visuoperceptive and visuoconstructive ability, and perceptual-motor speed. Age-related differences in general intelligence and visual memory in our sample of healthy men, ranging in age from 20 to 83 years, were found to be smaller than the differences reported in normative studies of non-health-screened adults. Visual memory and the discrepancy between verbal and visuospatial ability were not correlated with regional cerebral metabolic rates for glucose (rCMRglc) as measured by positron emission tomography (PET) and $^{18}$-Fluorodeoxyglucose.

In Alzheimer's disease the discrepancy between verbal and visuospatial abilities was found to be correlated with lateral asymmetry of cortical rCMRglc. Asymmetry of visual attention to the right and left sides of extrapersonal space was also related to lateral cerebral metabolic asymmetry. Older Down syndrome adults perform worse on mental abilities tests than do younger subjects. Immediate verbal memory appears to be less affected by age in Down syndrome than are other abilities.

Correlations between clinical, factor and localization scales in the Luria-Nebraska Neuropsychological Battery and lobar rCMRglc demonstrated statistically significant relations between metabolic deficits in the parietal lobe and reduced neuropsychological function subserved by the parietal lobe, in subjects with mild-moderate Alzheimer's disease but not in healthy controls.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00131-02 LN

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Neurological Function in Aging and Dementia

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | |
|---|---|---|
| C.L. Grady | Psychologist | LN NIA |
| A.D. Kay | Medical Staff Fellow | LN NIA |
| J.W. Renfrew | Psychologist | LN NIA |
| A. Moore | Social Worker | LN NIA |

COOPERATING UNITS *(if any)*

Research Services Branch, NIMH
Outpatient Department, Clinical Center

LAB/BRANCH

Laboratory of Neurosciences

SECTION

Brain Aging and Dementia

INSTITUTE AND LOCATION

NIA, NIH, Bethesda, Maryland 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.9 | 1.7 | 1.2 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Research was carried out on motor function in man in relation to aging and disease. With the use of a patient activity monitor worn on the non-dominant wrist in 14 healthy men for a period of 10 days, it was demonstrated that average wrist motor activity was lower in older individuals, primarily as a result of low activity during daytime hours. Sleep duration could be estimated from the analysis, and was not correlated with age.

A quantitative neurological examination was standardized in healthy men between 20 and 80 years of age, and established curves for age related declines in coordination, speed and accuracy of movement.

There was significant correlation between age and peripheral hearing sensitivity in healthy men, particularly at high frequencies, but when the effects of hearing loss due to age were taken into account, measures of speech discrimination and tympanometry were not related significantly with age.

In patients with Alzheimer's disease, studies of central auditory function using the staggered spondaic word (SSW) test indicated that a unilateral deficit was associated with temporal lobe atrophy on the contralateral cerebral hemisphere, as measured with CT scans, but not with asymmetry of cerebral glucose utilization.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 AG 00132-02 LN

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Brain Anatomy and Chemistry in Aging and Dementia

PRINCIPAL INVESTIGATOR *(List other professionel personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | |
|---|---|---|
| H. Creasey | Visiting Associate | LN NIA |
| A. Kay | Medical Staff Fellow | LN NIA |
| M. Schapiro | Medical Staff Fellow | LN NIA |

COOPERATING UNITS *(if any)*
Computer Systems Laboratory, Division of Computer Research Technology
Department of Pharmacology, Univ. of Pittsburgh School of Medicine
Department of Neurochemistry, NIMH

LAB/BRANCH
Laboratory of Neurosciences

SECTION
Brain Aging and Dementia

INSTITUTE AND LOCATION
NIA, NIH, Bethesda, Maryland 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3.0 | 3.0 | 0 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Computer assisted tomography (CT), together with three dimensional image reconstruction procedures, demonstrated in 30 healthy men between the ages of 21 and 81 yr, that the volume of cerebrospinal fluid increased in relation to age and that the volume of gray matter was correlated negatively with age, whereas the volume of white matter in the brain was age invariant. Even in healthy subjects, brain atrophy occurs with aging. The volumetric analysis technique also demonstrated brain atrophy, above and beyond that noted with respect to healthy aging, in subjects with Alzheimer's disease, as well as dilatation of cerebrospinal fluid spaces. The degree of atrophy was related to psychometric scores for dementia and mental competence. On the other hand, volumetric CT analysis demonstrated no differences, as compared with age matched controls, in brain morphometrics for adults with autism and for young adults with Down syndrome (after data were normalized to height).

Cerebrospinal fluid concentrations of homovanillic acid, 5-hydroxyindoleacetic acid, norepinephrine and 3-methoxy 4-hydroxyphenylethylne glycol did not differ significantly between patients with Alzheimer's disease and age-matched controls, and were not correlated with age in healthy controls. On the other hand, spinal fluid concentrations of choline increased with age in healthy controls, and were higher in young adults with Down syndrome than in age matched controls.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00133-02 LN

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less Title must fit on one line between the borders.)*
Clinical Pharmacokinetics, Pharmacodynamics and Therapeutics

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| N.R. Cutler | Section Chief | LN | NIA |
| A.D. Kay | Medical Staff Fellow | LN | NIA |

COOPERATING UNITS *(if any)*
Pharmacy Department, Clinical Center

LAB/BRANCH
Laboratory of Neurosciences

SECTION
Brain Aging and Dementia

INSTITUTE AND LOCATION
NIA, NIH, Bethesda, Maryland 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.6 | 1.0 | 0.6 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

1) Vancomycin's half life of the terminal phase is significantly prolonged in the elderly from young normals. No significant change was observed in volume of distribution which could be accounted for by altered tissue binding.

2) Zimelidine, a serotonergic reuptake blocker, was evaluated in Alzheimer's disease patients. Pharmacokinetic, neurochemical and neuropsychological effects were examined. The drug significantly reduced (by up to 38%) 5-hydroxy-indolacetic acid concentrations in cerebrospinal fluid (CSF). CSF concentrations of 3-methoxy-4-hydroxy-phenylglycol, a major metabolite of norepinephrine, tended to increase slightly. Overall, there was no effect of Zimelidine on memory function.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00134-01 LN

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Brain Lipid Metabolism, Relation to Function and Aging

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| J. Gnaedinger | Staff Fellow | LN | NIA |
| J. Miller | Staff Fellow | LN | NIA |

COOPERATING UNITS *(if any)*

LAB/BRANCH
Laboratory of Neurosciences

SECTION
Cerebral Physiology and Metabolism

INSTITUTE AND LOCATION
NIA, NIH, Bethesda, MD 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| | 2 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A method was developed to determine rates of incorporation of palmitic acid into different brain regions in the awake rat. The regional cerebral metabolic rate for palmitate, $rCMR_{palm}$, was determined. $rCMR_{palm}$ ranged from 2 x 10-5 mol/g-sec at the internal capsule to 9.3 x 10-5 mol/g-sec at the median eminence, and was proportional to the regional cerebral metabolic rate for glucose. $rCMR_{palm}$ is a measure of turnover of structural brain lipids in vivo.

In Fischer-344 rats at different ages, $rCMR_{palm}$ declines between 1 and 3 months, when myelination also declines, but is age invariant between 3 and 34 months. The latter findings indicates maintenance of cerebral integrity in the absence of disease. $rCMR_{palm}$ is independent of cerebral blood flow. It is unaffected by acute visual or auditory deprivation in awake rats, but is reduced by anesthesia induced by pentobarbital.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 AG 00135-01 LN

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Brain Protein Synthesis; Aging and Dementia

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J.W. Cosgrove Senior Staff Fellow LN NIA

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Neurosciences

SECTION

Cerebral Physiology and Metabolism

INSTITUTE AND LOCATION

NIA, NIH, Bethesda, MD 20205

| TOTAL MAN-YEARS: 1 | PROFESSIONAL: 1 | OTHER: 0 |
|---|---|---|

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Amino acid incorporation was measured in a cell-free protein synthesis system derived from brains of male Fischer-344 rats of different ages. This system has the capacity to initiate protein synthesis in vitro. There was no significant correlation between protein synthesis and age.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00136-01 LN

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Functional Interactions Among Brain Regions

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| B. Horwitz | Senior Staff Fellow | LN | NIA |
| R. Duara | Medical Staff Fellow | LN | NIA |

COOPERATING UNITS *(if any)*

LAB/BRANCH

Laboratory of Neurosciences

SECTION

Cerebral Physiology and Metabolism

INSTITUTE AND LOCATION

NIA, NIH, Bethesda, MD 20205

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 2 | 0 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A matrix method was developed to examine functional interactions between brain regions, by correlating the cerebral metabolic rates for glucose as determined by positron emission tomography in humans. The method was applied to regional metabolic data from 40 healthy men at rest, and demonstrated correlations among homologous regions between the cerebral hemispheres, and between the frontal and the parietal lobes on the one hand and the temporal and occipital lobes on the other. Furthermore, right-hemispheric regional interactions exceeded those in the left hemisphere.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 AG 00161

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Aging and Cell Structure

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J. E. Johnson, Jr., Acting Section Chief, EMS

COOPERATING UNITS *(if any)*

Laboratory of Neurosciences, NIA; University of Tampere, Tampere, Finland; Department of Pathology, Baltimore City Hospitals; Department of Biology, Dartmouth University.

LAB/BRANCH

Office of the Scientific Director

SECTION

Experimental Morphology

INSTITUTE AND LOCATION

NIA, NIH, Gerontology Research Center, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.5 | 1.5 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects
☐ (a1) Minors
☐ (a2) Interviews
☒ (b) Human tissues (and Animal Tissues)
☐ (c) Neither

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The superior cervical ganglia (SCG) of rats ranging in age from 4 to 35 months were examined by light and electron microscopy. The specimens were fixed by perfusing the rats with a buffered aldehyde fixative, the ganglia removed, post-fixed, dehydrated, and embedded in epoxy. Thick sections were stained with toluidine blue for light microscopy, while thin sections for electron microscopy were stained with uranyl acetate and lead citrate. The ganglion cells of young animals contained cytoplasmic lysosomes, most of which would be classified as primary. With increasing age, lipofuscin began to accumulate, often confined to one region of the cytoplasm. Neurozxonal Dystrophy (NAD) was a striking feature of older rats. The NAD was characterized by arrays of membranes, patches of electron lucent material, and mitochondria in the condensed configuration. Nuclear inclusions were present in the ganglion neurons of aging animals as well. In comparing the NAD found in the superior cervical ganglion with NAD seen in our studies of the central nervous system, we observed that the membrane arrays of the SCG were different in morphology from arrays seen in the dorsal column nuclei of aging mice. Secondly, mitochondria of NAD in the dorsal column nuclei were enlarged, while mitochondria of NAD in the SCG tended to be condensed. Our studies thus indicate that Neuroaxonal Dystrophy, although a single classification of neurological deterioration which affects every vertebrate, including man, must be sub-classified according to the particular nervous system region under study.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00162

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Electron Microscopy of Human Brain Aging and Dementia.

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J. E. Johnson, Jr., Acting Section Chief, EMS

COOPERATING UNITS *(if any)*

Laboratory of Neurosciences, NIA
University of Tampere, Tampere, Finland

LAB/BRANCH

Office of the Scientific Director

SECTION

Experimental Morphology

INSTITUTE AND LOCATION

NIA, NIH, Gerontology Research Center, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 1 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Autopsy specimens were obtained from the nervous system of human patients, some of whom were diagnosed as having Alzheimer's disease, and some of whom served as controls. The specimens were placed in buffered aldehyde fixative as soon after death as possible, and subsequently processed for light and electron microscopy. At present, we have examined the stellate ganglia (part of the autonomic nervous system). Ganglion neurons were found to contain large amounts of lipofuscin granules, some of which were as large as 4 microns in diameter. Lewy bodies were present in one Alzheimer's patient. The Lewy bodies consisted of filament masses, with the filaments arranged in varying directions at the center, and radially at the periphery. None of the filaments seen so far in the stellate ganglia were of the paired helical filament (PHF) type. Ringed inclusions, typical of Neuroaxonal Dystrophy (NAD) were also seen in neuronal somata and cell processes. The preliminary results of this ongoing study indicate that structural features characteristic of Alzheimer's disease may be different in the autonomic nervous system than in the central nervous system.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00163

PERIOD COVERED: October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*: Electron Microscopy of Aging and Drug Abuse

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J. E. Johnson, Jr., Acting Section Chief, EMS

COOPERATING UNITS *(if any)*: National Institute on Drug Abuse, Baltimore, Maryland
University of Tampere, Tampere, Finland

LAB/BRANCH: Office of the Scientific Director

SECTION: Experimental Morphology

INSTITUTE AND LOCATION: NIA, NIH, Gerontology Research Center, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 1 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

(Animal Tissues)

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Rats were treated with either morphine or placebo by implantation of subcutaneous pellets. After one week, morphine-treated rats were addicted, as demonstrated by naloxone-induced abstinence. The animals were sacrificed by perfusion with buffered aldehyde fixative. The superior cervical ganglia (SCG), kidneys, and other tissues were removed and processed for light and electron microscopy. In the SCG, the percentage of secondary lysosomes, compared to primary lysosomes, was higher in the morphine-treated rats than in control rats ($p<0.05$). There was a strong trend ($0.1>p>0.05$) for the range of mitchondrial diameters to increase, suggesting that some mitochondria were enlarged and others were condensed in morphine-treated rats. In the kidney, both short ($p<0.05$) and long ($p<0.01$) microvilli increased in frequency on the surface of glomerular podocytes following morphine treatment. These results strongly resemble those obtained in studies of the aging superior cervical ganglion and kidney, and suggest that morphine can cause ultrastructural alterations which mimic changes normally occurring with age.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00202-1 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Physical Activity, Fitness Levels, Age, and Risk Factors

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Andrzej Ziemba, Ph.D. Visiting Fellow
Reubin Andres, M.D. Chief, Metabolism Section, CPB, NIA

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Metabolism Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.75 | 0.95 | 0.8 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Volunteers in the Baltimore Longitudinal Study of Aging complete a detailed activity history questionnaire on most visits. A coding system has been developed which results in the computation of an average daily caloric expenditure value. In addition, these subjects perform maximal treadmill exercise tests. In the past few years, the maximal work equivalent is known (treadmill speed and slope) and maximal oxygen consumption is measured. Thus measures are available for general activity levels and for degree of physical conditioning. These estimates are being entered into a multiple regression program to evaluate their roles in determining blood pressure and serum lipid levels and glucose tolerance in BLSA subjects.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00203-1 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Body Weight, Fat Distribution Pattern and Mortality in the Baltimore Longitudinal

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*


Patricia Coon, M.D. Medical Staff Fellow
Andrzej Ziemba, Ph.D. Visiting Fellow
Reubin Andres, M.D. Chief, Metabolism Section, CPB, NIA


COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Metabolism Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.9 | 0.7 | 1.2 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*


Overweight is known to be associated with hypertension, hyperlipidemia, and hyperglycemia. Recently, two groups of investigators have shown that the distribution of body fat can be measured by the ratio of waist to hip girth (WG/HG). Data in normal men (as opposed to obese men) are limited to residents of Goteborg born in the year 1910. Our BLSA data then offers a unique opportunity for assessing WG/HG as a risk factor. Our analyses to date have included both bivariate and multiple regression techniques to assess interrelations among age, overweight (the Body Mass Index, BMI), and WG/HG on serum cholesterol (CH), triglyceride (TG), glucose tolerance (GT), and systolic and diastolic blood pressure. Glucose tolerance analysis to date has been that obtained since 1977 using essentially the currently accepted recommended glucose dose (40 $g/m^2$ surface area or, usually, about 75 grams). Since the distribution of TG values are log-normally distributed, analyses were made against log TG. Furthermore, the relationship of age to TG and to CH is not a simple linear one but is instead best described as an inverted U-shaped curve; it was therefore necessary to use Age and $Age^2$ as independent variables. The results showed a very strong association of age with WG/HG. In fact even into old age, WG/HG continues to increase although the BMI decreases. There is thus apparently a continuing redistribution of body fat from periphery to core (abdomen) with aging. Also WG/HG increases directly with increasing BMI at all ages. Thus, the multiple regression technique is essential for the determination of independent effects of these variables on the dependent variables. This analysis showed highly significant effects of fat distribution on the metabolic variables (CH, TG, and GT) but very little effect on BP. On the contrary, overweight, as judged by the BMI, had a highly significant effect on BP but not on the metabolic end-points. These results hold for young and middle-aged men and for the "young-old" (55-74 yr). The dependent risk factors in the "old-old" (75-96 yr) seem to be generally uninfluenced either by fatness or by its distribution pattern.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00204-1 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

The Effect of Glucose Tolerance and Age on Risk Factors, Morbidity, and Mortality

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Reubin Andres, M.D. Chief, Metabolism Section, CPB, NIA
Andrzej Ziemba, Ph.D. Visiting Fellow

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Metabolism Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3.15 | 0.35 | 2.8 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The first comprehensive analysis of normative oral glucose tolerance data using essentially the National Diabetes Data Group recommended glucose dose has been completed. For simplicity, NDDG recommended 75g for all adults regardless of body size; we have used 40 g/$m^2$ surface area (our average BLSA male receives close to 80 g and our average BLSA female receives closer to 70 g). There is a progressive decrease in tolerance with age, the mean glucose levels being very similar to those of the larger glucose load test, but significantly lower. A new nomogram has been constructed which provides rapid age-adjusted evaluation of performance for men and for women. There is a significant sex difference; women have the better glucose tolerance. In addition to the two oral glucose tolerance tests, there has now been a 20 year follow-up of men given three other tests: IVGTT, cortisone GTT, and tolbutamide response test. Performances on all these tests are being compared by converting the usual interpretative scores (decay constants, glucose levels, and percent falls in glucose) into Z-scores. Effects of performance levels at different ages are being analyzed on serum lipid levels, blood pressure, and the development of overt diabetes, coronary artery disease, and on mortality.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00205-1 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Recommended Weight Tables: An Independent Analysis of Insurance Data

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Reubin Andres, M.D. Chief, Metabolism Section, CPB, NIA

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Metabolism Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.75 | 0.25 | 0.5 |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standerd unreduced type. Do not exceed the space provided.)*

A comprehensive analysis has been made of the mortality data published in tabular form in great detail by the Society of Actuaries in the Build Study 1979. Data are available on 5 age decades (20-29 through 60-69 yr) on both men and women. Mortality ratios (actual/expected deaths) were related to a large number of height-weight categories. These data provide the source for the computation of the widely accepted Metropolitan 1983 Tables. Examination of the Build Study data showed that the relation of the Body Mass Indices (BMI = $Wt/Ht^2$) to the Mortality Ratios (MR) was U-shaped and that a quadratic equation was required to fit the data accurately. Computations for each age-sex group were based on the following equation: $MR = a + b\,(BMI) + c\,(BMI)^2$. The equation (1) permits the construction of curves which accurately relate BMI to MR; (2) provides the value of BMI associated with minimal mortality (the nadir of the U-shaped curve); and (3) provides the range of BMI's associated with less than expected mortality (the two points at which the U-shaped curve intersects the 100 MR line). The BMI of minimal mortality was found to increase markedly with age. Furthermore, there were no significant differences between men and women. Thus the "best" BMI increases from 20.5 $kg/m^2$ at age 20-29 yr to 26.9 at age 60-69 yr. The recommended range of BMIs can be set at 18-23 $kg/m^2$ for 20-29 yr and increases linearly to 24-30 $kg/m^2$ for 60-69 yr old subjects. These values contrast sharply with those previously recommended (20-25). The 1983 Metropolitan Tables, (when heights and weights are converted to BMI) recommend essentially a range of 20-26 for men and women from age 25-59 years. The data show however that age cannot be neglected as a variable in the setting of recommended weight ranges.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00221-03 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Sodium-Calcium Dependence of Resting Force in Rat Cardiac Muscle

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: E. G. Lakatta Chief, Cardiovascular Section CPB, NIA

COOPERATING UNITS *(if any)*

Division of Cardiology, Department of Medicine, Johns Hopkins Hospital (G. Gerstenblith)

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.0 | 1.0 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In unstimulated isolated, rat ventricular muscle, the increase in resting force ($\Delta RF$) which occurs with an increase in external calcium concentration ($\Delta[Ca^{2+}]_e$ can be largely abolished by lowering cellular sodium content by removing sodium from the perfusate and can be potentiated by raising cellular sodium content by adding ouabain. We hypothesized that this demonstrated the activity of a membrane Na/Ca exchange (see Z01 AG 00221-02 CPB). Since this membrane exchange is well known to exhibit graded activity, we sought to extend our observations by demonstrating a graded response between $[Na^+]_i$ and $\Delta RF$. External potassium concentration ($[K^+]_e$) was set at gradully lowered values for each experiment in the series to give graded inhibition of the Na-K pump and thus graded elevation of $[Na^+]_i$. $[Ca^{2+}]_e$ was then increased from 0 to 2 mM and the $\Delta RF$ recorded. The results shown that increasing RF occurs with decreasing $[K^+]_e$ (and thus increasing $[Na^+]_i$. Thus, not only does the $\Delta RF$ for a $\Delta[Ca^{2+}]_e$ depend on $[Na^+]_i$, but does so in a graded manner. This is further evidence for the activity of the Na/Ca exchange in controlling $\Delta RF$ in isolated rat muscle. In extending these studies to the intact heart we hypothesized that after a $Ca^{2+}$ free period the magnitude of the $Na^+$ gradient at the onset of $Ca^{2+}$ reperfusion would grade the ensuing cell $Ca^{2+}$ gain. Our results indicate that (1) myocardial cell $Na^+$ increases during $Ca^{2+}$ free perfusion and (2) the magnitude of the $Na^+$ gradient at the end of the $Ca^{2+}$ free period is an important determinant of the extent of cell $Ca^{2+}$ gain, cell $K^+$ loss, and reduction of contractile function with $Ca^{2+}$ reintroduction, which collectively have been referred to as the "calcium paradox" in the heart.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 AG 00222-03 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Altered Mechanical Properties in Myocardium from Rats Subjected to Food Deprivation

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | H. A. Spurgeon | Physiologist | CPB, NIA |
| Others: | E. G. Lakatta | Chief, Cardiovascular Section | CPB, NIA |
| | E. S. Beard | Chemist | CPB, NIA |
| | D. Ingram | Staff Fellow | LCMB, NIA |

COOPERATING UNITS *(if any)*

Department of Physiology, University of Ottawa, School of Medicine, Ottawa, Canada (K. Rakusan)

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.6 | 0.4 | 0.2 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*


Male Wistar rats were studied after caloric restriction by intermittant feeding alternating on a daily basis with free access to feed, (EOD), and compared to age matched controls. Morphology of left ventricular cells was determined by methods developed by Dr. Rakusan on tissue perfused in situ in our laboratory with buffered gluteraldehyde. Subsequent light microscopic measurements showed both mean and median % tissue as capillaries are not significantly reduced by EOD feeding after 24 months on trial, as compared to adult controls on normal diet (5.46 $\pm$ 0.66% vs. 4.98 $\pm$ 2.96%) but there is a significant reduction in 30 month animals (3.3 $\pm$ 0.4%) with $p < .02$ comparing 30 month EOD to 24 month, and $p < .05$ compared to adults. Cell diameter is singificantly reduced with increasing age. Adult myocardial cells average 28.9 $\pm$ 0.74 $\mu$m, compared to 25.76 $\pm$ 0.56 $\mu$m for 24 month EOD, $p < .02$. A further reduction to a mean of 23.2 $\pm$ 0.8 um was found at 30 months in EOD animals, (comparing 24 month EOD to 30 month EOD, $p < .05$). Isolated trabecular muscle responsiveness to superfused catecholamines appears to be preserved throughout the age range, while the senescent control animals at 24 months show a loss in responsiveness consistant with reports from this and other laboratories.

Thus, EOD feeding appears to protect function, preventing the reduction in responsiveness to catecholamines even though the contraction duration which is a hallmark of cardiac muscle aging is quantitatively identical in the 20 month controls and 24 month EOD muscles. Morphologically there is no difference in the two groups of animals at 24 months except for reductions in the percentage of tissue as capillaries and in the diameter of cardiac muscle cells.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00223-03 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Effect of Age on the Components of Atrioventricular Conduction in Normal Man

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | J. L. Fleg | Staff Cardiologist | CPB, NIA |
| Others: | E. G. Lakatta | Chief, Cardiovascular Section | CPB, NIA |

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.4 | 0.3 | 0.1 |

CHECK APPROPRIATE BOX(ES)

☒(a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have utilized a signal averaging, high resolution ECG to record His bundle potentials from the body surface of 111 normal Baltimore Longitudinal Study (BLS) volunteers ages 21 to 79. By allowing measurements of conduction time both proximal and distal to the bundle of His, this technique should enhance our understanding of the age-related changes in the cardiac conduction system. In 52 women, neither PR nor HV interval was related to age. In 59 men, the following age relationships were found:

| | | |
|---|---|---|
| PR interval | = 142.4 msec + .477 age | .388 <.01 |
| PH interval | = 105.3 msec + .427 age | .393 <.01 |
| PR segment | = 47.6 msec + .315 age | .328 <.02 |
| Proximal PR segment | = 10.5 msec + .267 age. | 330 <.02 |

Thus, an age-related prolongation of PR interval is found only in men and appears to be due largely to a delay in the proximal PR segment, presumably reflecting delay within the atrioventricular junction.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00224-03 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Cardiac Myofibrillar ATPase Activity Across a Broad Age Range

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | M. B. Effron | Senior Staff Fellow | CPB, NIA |
| Others: | G.M. Bhatnagar | Guest Researcher | CPB, NIA |
| | E. S. Beard | Chemist | CPB, NIA |
| | E. G. Lakatta | Chief, Cardiovascular Section | CPB, NIA |

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.5 | 1.5 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

As previously reported, myofibrillar ATPase activity and the duration of the isometric twitch in papillary muscles change with age and do not appear to be related. Maximum myofibrillar ATPase activity in detergent treated myofibrils decreased approximately twofold in rats between 2 and 6 months of age while the contraction duration of the isometric twitch increased progressively across the age span changing by approximately 30% in rats 24 months of age. It has been reported that animals treated with thyroxine increased the myosin ATPase activity and decreased the time to peak force, a component of twitch duration, and have suggested that the two parameters are related. Therefore, we treated young (2 mo), adult (8 mo), and senescent (24 mo) rats with thyroxine to produce a hyperthyroid state and were able to show that the contraction duration of the isometric twitch decreased without altering the maximum ATPase activity in any group. However, when myosin isoenzymes V1, V2, and V3 were examined, a redistribution of these isoenzymes occurred both with age and thyroxine treatment. Therefore, we conclude that age-associated prolongation of contraction duration is not fixed and can be reversed with thyroxine treatment. However, changes in myofibrillar ATPase activity are not associated with the changes in contraction duration produced by alterations of the thyroid state of the rat while changes were seen in the myosin isoenzyme pattern. This suggests that myosin ATPase and not myofibriallar ATPase may play an important role in contraction duration.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00225-02 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Effect of Age on Isolated Muscle Function in Spontaneously Hypertensive Rats

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | | |
|---|---|---|---|---|
| PI: | G. D. Walford | Staff Fellow | DOD 7/01/83 | CPB, NIA |
| Others: | E. G. Lakatta | Chief, Cardiovascular Section | | CPB, NIA |

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| | | |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The spontaneously hypertensive rat (SHR) develops sustained arterial hypertension at a young age, progressive cardiomegaly, and has a high incidence of cardiovascular deaths at an age younger than its non-hypertensive control strain. It is thus an attractive model for the study of the interaction of aging and "disease." The results presented here show that (1) intra-arterial blood pressure in the SHR is elevated at 5 months compared to controls and this is sustained until 21 months; (2) cardiomegaly is 110% at 5 months and 143% at 21 months; (3) isolated muscle at 29°C shows an interaction of age and "disease" for several parameters: (a) contraction duration, (b) developed force at short muscle lengths or in response to changes in the pattern of stimulation, and (c) recovery from hypoxia. Thus there are several important interactions of age and "disease" which are manifest in the performance of isolated cardiac muscle.

Discontinued.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00226-02 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Excitation-Contraction in Isolated Cardiac Cells

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | M. C. Capogrossi | Staff Fellow | CPB, NIA |
| Others: | E. G. Lakatta | Chief, Cardiovascular Section | CPB, NIA |

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 0.8 | 1.2 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have dissociated myocardial muscle cells from adult rats and rabbits. These preparations are being used to study the contractile, electrophysiological, and biochemical characteristics in a variety of different conditions. In particular we have been able to identify in these isolated cells a longitudinally propagating wave which occurs spontaneously when the cell is not being electrically stimulated and is considered at rest and has a normal resting membrane potential. These "waves" are likely to represent the phenomenon of calcium induced calcium release (CICR) and are the cause of the scattered light intensity fluctuations (SLIF) which our laboratory has studied in the past in multicellular preparations. With our work we have attempted to validate single cells as a model for the study of mechanisms of excitation-contraction coupling and in particular of CICR.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 AG 00227-02 CPB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Excitation-Contraction in Rat Myocardium: Alterations with Adult Aging

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | E. G. Lakatta | Chief, Cardiovascular Section | CPB, NIA |
| Others: | C. Orchard | Visiting Fellow | CPB, NIA |

COOPERATING UNITS *(if any)*

LAB/BRANCH

Gerontology Research Center, Clinical Physiology Branch

SECTION

Cardiovascular Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.5 | 0.5 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have studied the effect of age on the increase of cytoplasmic $[Ca^{2+}]$ which initiates contraction in the heart muscle (the calcium transient). Right ventricular papillary muscles from the hearts of young adult and senescent rats were microinjected with the photoprotein aequorin, which emits light as a function of $[Ca^{2+}]$. Tension development and intracellular $Ca^{2+}$ were monitored simultaneously. The time to peak developed tension, and the half time of relaxation of tension, were longer in the muscles from the senescent animals than in the muscles from the young animals. The half time of the decline of the calcium transient, which depends on the rate at which $Ca^{2+}$ is removed from the cytoplasm, was also slower in the muscles from the senescnet animals. These results give more direct evidence than has been available previously that the longer contraction duration in senescent myocardium may be due to slower $Ca^{2+}$ sequestration by the sarcoplasmic reticulum in the older muscle.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00228-01 CPB

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 chererters or less. Title must fit on one line between the borders.)*
Complications of Maximal Treadmill Exercise in Apparently Normal Subjects

PRINCIPAL INVESTIGATOR *(List other professionel personnel below the Principal Investigetor.) (Neme, title, leboretory, and institute affiliation)*


| | | | |
|---|---|---|---|
| PI: | J. L. Fleg | Staff Cardiologist | CPB, NIA |
| Others: | E. G. Lakatta, | Chief, Cardiovascular Section | CPB, NIA |


COOPERATING UNITS *(if eny)*

LAB/BRANCH
Gerontology Research Center, Clinical Physiology Branch

SECTION
Cardiovascular Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.4 | 1.4 | |

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the spece provided.)*


We have assessed the prevalence of exercise-induced ventricular tachycardia, exercise-induced supraventricular tachycardia and post-exercise hypotension in BLSA volunteers without clinical evidence of heart disease.

Out of 925 subjects undergoing maximal treadmill exercise between September, 1977 and December, 1983, 10 subjects (1.2%) developed nonsustained ventricular tachycardia (VT) during or after exercise. Episodes varied in length from 3 to 6 beats and were never associated with symptoms. The prevalence of VT was 3.8 % in subjects aged 65 and older. Over a follow-up period averaging 2.0 years, no subject with exercise-induced VT developed syncope, pre-syncope, angina, myocardial infarction or sudden death.

Exercise-induced supraventricular tachycardia (SVT) occurred in 50 subjects (5.3%). All episodes were paroxysmal atrial tachycardia; heart rate varied from 120 to 250 bpm ($\bar{x}$ = 175 $\pm$ 40). Of the 70 episodes of SVT, only 12 were $\geq$ 10 beats in length; 4 of these were associated with symptoms. The prevalence of SVT was 12.7% in the 245 subjects $\geq$ 65 years old but only 2.7% in those < 65 years. An ischemic ST segment response to exercise occurred in 14% of subjects.

Hypotension following treadmill exercise, defined by a fall in systolic blood pressure (SBP) at least 20 mm Hg below sitting pre-exercise level to a value < 90 mm Hg , occurred in 15 subjects (1.7%) with a mean age of 44.2 years. Bradycardia was associated with hypotension in only 3 subjects. When compared with age-matched controls, hypotensive subjects had higher maximal heart rates (183.9 $\pm$ 14.7 vs 173.1 $\pm$ 11.2 bpm) but no difference in SBP at submaximal or maximal effort. Post-exercise ST segment abnormalities suggestive of myocardial ischemia occurred in one third of the hypotensive subjects but none of the controls, $p<.05$.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00229-01 CPB

PERIOD COVERED
October 1 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Age-Related Changes in Adrenergic and Cholinergic Responses in Rat Atria

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

| | | | |
|---|---|---|---|
| PI: | M. McIvor | Medical Staff Fellow | CPB, NIA |
| Others: | E. G. Lakatta | Chief, Cardiovascular Section | CPB, NIA |

COOPERATING UNITS *(if any)*

LAB/BRANCH
Gerontology Research Center, Clinical Physiology Branch

SECTION
Cardiovascular Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| .6 | .6 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

While the effects of age on the adrenergic responsiveness of cardiac ventricular tissue has been delineated, data is scanty on how age may affect the cholinergic modulation of these adrenergic effects. Neither adrenergic nor cholinergic modulation of aged atrial tissue have been studied. Isolated transmural left atrial strips from adult (12 mo) and senescent (24) virgin male Wistar rats were stimulated isometrically at $L_{max}$ at 30°C in krebs buffer containing 0.5 mM $Ca^{+}$. A dose response relationship to progressively greater concentration of isoproterenol ($10^{-12}$ to $10^{-6}$ M) was established for both groups. A progressive dose response relationship was similarly established for acetylcholine ($10^{-10}$ to $10^{-3}$ M) in atria superfused with Krebs already containing $10^{-6}$ isoproterenol. Changes in time to peak force, total developed tension, resting tension, contraction duration, and maximal rate of force development were measured. While age-related changes in time to peak force and contraction duration were found, an initial analysis of the data failed to shown any age-related changes in adrenergic responsiveness as measured by these parameters. However, the developed tension in isoproterenol-potentiated senescent atria was more sensitive to suppression by acetylcholine.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 AG 00241-03 CPB

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Development of Statistical Methodology for the Analysis of BLSA Data

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
*(Name, title, laboratory, and institute affiliation)*

Larry J. Brant Mathematical Statistician CPB NIA

COOPERATING UNITS *(if any)*

David B. Duncan Mathematical Statistician (IPA) CPB NIA
Department of Biostatistics, Johns Hopkins University
Dean S. Bross Mathematical Statistician (IPA) CPB NIA
Department of Preventive Medicine, University of Maryland

LAB/BRANCH
Gerontology Research Center, Clinical Physiology Branch

SECTION
Human Performance Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.6 | 1.4 | 0.2 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The theoretical development of statistical methodology is progressing in the areas of epidemiological models, multiple comparisons and survival analysis, each of which is applicable to longitudinal studies. The research utilizes Bayesian theory and various regression methods for prospective studies. The methodology created provides original contributions to experimental testing of the simultaneous comparison of specified effects (e.g. treatments against a control or placebo), epidemiological study of disease states, survival or failure analysis of longitudinal data and other longitudinal observations representing growth and other physical changes of humans and animals. Accomplishments in the creative use of Bayesian theory in the area of multiple comparisons will fill a void in the established statistical armamentarium.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 AG 00242-03 CPB

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Female Sexuality, Menopause, and Aging

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*

| *(Name, title, laboratory, and institute affiliation)* | | |
|---|---|---|
| Frances E. Purifoy | Staff Fellow | CPB NIA |

COOPERATING UNITS *(if any)*

| | | |
|---|---|---|
| Jordan D. Tobin | Chief, Human Performance Section | CPB NIA |
| Clyde E. Martin | Sociologist, Human Performance Section | CPB NIA |

LAB/BRANCH
Gerontology Research Center, Clinical Physiology Branch

SECTION
Human Performance Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| | | |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The study of age and menopause-related variability in female sexual behavior was initiated in May, 1982; data is obtained by personal interview from each female participant of the Baltimore Longitudinal Study of Aging. To date, 156 (98% of those asked to participate) interviews have been done. A two-stage analysis of data from the first 130 cases involved contingency table comparisons of a pre-menopausal group aged 20-43, a middle group aged 45-55, and a post-menopausal group aged 56-79 as well as contrasts among those aged 20-39, 40-59, and 60-79 years. Focus thus far has been on 1) Age and menopause related variability in current sexual enjoyment, satisfaction, degree of arousal, adequacy of lubrication, frequency of orgasm as well as change in these measures over each women's sexual life; and 2) Birth-Cohort Contrasts in pre-marital and marital sexual behavior and current sexual attitudes - which presumably reflect variation in the socio-cultural background of the three age groups.

Dr. Purifoy left in December 1983 and interviews have been terminated. The data has been stored on the computer, initial analysis performed, and the manuscripts are currently being prepared.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00301-1 LCMB

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.) Regulation of Physiological Functions During Aging: I. Hormone and Neurotransmitter Action

PRINCIPAL INVESTIGATOR (List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)

G. S. Roth, Chief, Molecular Physiology & Genetics Section, LCMB, NIA

Other:

| | | | | |
|---|---|---|---|---|
| M. Shiraki | Visiting Associate | MPGS | LCMB | NIA |
| R. Chuknyiska | Visiting Fellow | MPGS | LCMB | NIA |
| J. Henry | Staff Fellow | MPGS | LCMB | NIA |
| M. Blackman | Guest Scientist | ES | CPB | NIA |
| J. Rifkind | Research Chemist | IBS | LCMB | NIA |

COOPERATING UNITS (if any)
B. Baum, Dental Officer, PCB, National Institute of Dental Research

LAB/BRANCH
Laboratory of Cellular and Molecular Biology

SECTION
Molecular Physiology and Genetics Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3.0 | 2.5 | .5 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

This project is mainly involved in elucidating those mechanisms by which the ability of hormones and neurotransmitters to regulate physiological functions is altered during aging.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

# NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 AG 00302-1 LCMB

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.) Regulation of Physiological Functions During Aging: II. Behavioral Biology

PRINCIPAL INVESTIGATOR (List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)

Donald K. Ingram, Senior Staff Fellow, Lab. of Cellular & Molecular Biology, NIA

Other:

| | | | | |
|---|---|---|---|---|
| G. S. Roth | Research Chemist, Chief, MPGS | | LCMB | NIA |
| R. Cutler | Research Chemist | MPGS | LCMB | NIA |

COOPERATING UNITS (if any) E. London, Addiction Research Center, NIDA; D. Olton, Dept. of Psychology, Johns Hopkins University; D. Harrison, The Jackson Laboratory; H. Altmann, Lafayette Clinic; and E. Bresnahan, Essex Community College

LAB/BRANCH
Laboratory of Cellular and Molecular Biology

SECTION
Molecular Physiology and Genetics Section

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.0 | 1.2 | .8 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

The purpose of this project is to assess the effects of aging at a behavioral level of analysis in animal models, to identify neurobiological mechanisms associated with these effects, and to test interventions which might alter age-related performance decrements. Rodent models are tested in a battery of motor and learning/memory tasks. Neurochemical assays are conducted to determine neurobiological correlates of functional losses. Interventions include dietary restriction, environmental enrichment, and various pharmacologic treatments. Multiple genotypes are examined to determine possible genetic involvement in the pattern of age-related behavioral impairment.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER: Z01 AG 00303-1 LCMB

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)* Regulation of Physiological Functions During Aging: III Gene Expression and the Biology of Human Longevity

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Richard G. Cutler, Research Chemist

COOPERATING UNITS *(if any)*

Dr. Richard Setlow, Brookhaven National Laboratory, Director of Biology Department, Upton, L.I., N.Y.
Dr. Donald K. Ingram, Senior Staff Fellow, Molecular Physiology & Genetic Section Gerontology Research Center, NIA

LAB/BRANCH

Laboratory of Cellular and Molecular Biology

SECTION

Molecular Physiology and Genetics Section

INSTITUTE AND LOCATION

NIA, NIH, Baltimore, Maryland 21224

| TOTAL MAN-YEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.2 | 1.0 | .2 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Humans have a significantly higher resistance to aging than any other mammalian species. Our general research objective has been to understand the biological basis of this resistance. The research program involves three inter-related projects, entitled: (1) Stability of Proper Gene Expression, (2) Mechanisms Causing Improper Gene Expression and (3) Stabilizing Mechanisms of Proper Gene Expression. Past work involving the first two projects has found evidence that proper gene expression is not maintained with increasing age of an animal. The mechanism causing this improper gene expression may involve specific types of chromatin alterations, as evidenced by our findings of altered chromatin physiochemical properties. Recent work has centered on the third project, the mechanisms stabilizing proper gene expression. We have been examining the possibility that normal tissue antioxidants may help to stabilize the differentiated state of cells and may therefore be important determinants of human longevity. These antioxidants include superoxide dismutase, urate, alpha tocopherol, and the carotenoids, which show a good positive correlation with maximum life span potential of mammalian species. However, no correlation was found for ascorbate, and a negative correlation was found for glutathione, glutathione peroxidase, glutathione S-transferase and catalase, indicating that these enzymes may have toxic side effects previously not recognized. The rate of tissue homogenates autoxidizing in air, forming lipid peroxides, has been found to be inversely related to the maximum lifespan potentials of a number of different mammalian species. Taken together, these results indicate that aging is a result of cellular dysdifferentiation and that specific antioxidants and the structural composition of cells determine net sensitivity of tissue to the toxic effects of oxygen radicals and consequently the stability of cells against dysdifferentiation. Thus, longer-lived species have, in proportion to their longevity, more of these protective mechanisms which could appear to act importantly in stabilizing proper gene expression.

CONTRACT

Name and Number: JOHNS HOPKINS UNIVERSITY (N01-AG-7-2129)

Title: Non-invasive Assessment of Cardiac Structure and Function in Aging Men and Women

Date Contract Initiated: September 30, 1977

Current Annual Funding Level: About $200,000.00

Objectives:

A. Two-dimensional echocardiography is a relatively new technical development which allows determination of cardiac anatomy and function in much the same manner as routine echocardiography, with the important addition that an entire plane of the heart can be visualized at once rather than a simple "ice pick" view, allowing greater accuracy in the determination of heart chamber shape, size and function. The initial goal was to examine subjects from the Baltimore Longitudinal Study over a five year period (ages 18-95) during rest and maximal semi-supine bicycle exercise to determine age-related differences in regional and global myocardial function.

B. Beginning in FY 81 multi gated acquisition MUGA scans were obtained both at rest and during exercise in subjects of all ages. This newly developed technique, which utilizes $^{99m}$Technetium as a tracer provides as much infomation during exercise as the two-dimensional echocardiogram, but has the distinct advantage that the yield of technically satisfactory studies approaches 100% (vs 15%) overall for the ultrasound technique.

C. Thallium$^{201}$ myocardium imaging allows non-invasive assessment of regional left ventricular blood flow combined with stress ECG and will be used to determine the incidence, severity, and prognostic implications of ischemic heart disease in Baltimore Longitudinal Study participants. The predictive values of this technique will be compared to that of stress electrocardiography and two-dimensional echocardiography.

D. Beginning in the fiscal year 81 a statistical analysis of the data influence of age on the development of ischemic heart disease was initiated. The specific goals of this analysis are: (1) to determine the prevalence, severity, and prognostic implications of ischemic heart disease in a normal aging population; (2) to determine whether age-related changes that occur in myocardial performance or structure and whether these changes are related to alterations in myocardial perfusion; (3) to determine the predictive value of electrocardiography, thallium$^{201}$ perfusion imaging and echocardiography during exercise stress with regard to subsequent events; and (4) to relate the presence of evidence of ischemic heart disease to the presence of specific or potential risk factors documented over a 20 year period in the study population by various investigators.

Major Findings:

A. Approximately 450 subjects have undergone two-dimensional echocardiography and this test has been phased out in FY 82. Analysis of the resting echocardiograms is in progress. Exercise tracings had been difficult to obtain, especially

in elderly subjects. The echocardiographic responses to supine bicycle exercise in young subjects (mean age 31 ± 1 yr) versus old subjects (mean age 64 ± 3 yr) have been compared and the data presented at the Annual Scientific Sessions of the American Heart Association. Although echo indices of end-diastolic area (EDA) and end -systolic area (ESA) did not differ between the two groups at rest, EDA increased in the old group during exercise whereas it remained unchanged in the young. ESA, however, decreased in the young during exercise but was unchanged in the elderly. These findings indicate distinct age-related differences in the mechanism of increasing stroke volume during exercise. The bulk of the echo data is currently being reduced for analysis.

B. To date 147 subjects have undergone bicycle stress MUGA's. Results indicate that older subjects are not able to increase their ejection fraction during exercise to the same extent as younger ones. The data also appear to confirm our two -dimensional echocardiographic findings that older subjects increase stroke volume during exercise primarily through a Frank-Starling mechanism whereas younger subjects do so by decreasing end-systolic volume. Another major finding is that, in spite of these differences during exercise, these active BLSA subjects carefully screened for coronary artery disease are able to maintain cardiac output both at rest and during exercise. We have also found that the age-associated reduction in resting radionuclide and echocardiographic-derived maximal diastolic filling rates is abolished during exercise, allowing older subjects to take full advantage of the Frank-starling mechanism. These results were presented in abstract form at the American Heart Association national meetings in 1981, 1982 and 1983.

C. Approximately 500 subjects have received exercise treadmill thallium$^{201}$ scintigrams. Thallium scanning has shown an increasing rate of positivity with age, even in asymptomatic subjects. We define latent coronary heart disease (CHD) only when either the exercise ECG or thallium scan is abnormal. Using these stress criteria (SC) and the resting criteria (RC) on standard ECG, we have defined the prevalence of CHD in an initial subset of the population in the table below.

| Age (yr) | 40's | 50's | 60's | 70's | 80's |
|---|---|---|---|---|---|
| N | 41 | 70 | 73 | 36 | 10 |
| RC | 0% | 13% | 15% | 22% | 20% |
| RC+SC | 0% | 24% | 37% | 56% | 50% |

These combined figures (RC+SC) agree closely with the prevalence of CHD found in autopsy studies and suggest that stress thallium scintigraphy may provide a useful tool to enhance the detection and epidemiology of CHD. In 235 BLSA participants free of clinical CHD, we have used the combination of the exercise ECG and thallium scintigraphy to predict the development of angina pectoris, myocardial infarction and sudden death. Only 3 such events occurred in 179 subjects in whom both tests were negative, whereas 5 events occurred in the 14 subjects in whom both tests were positive. By stepwise logistic regression, both age ($x^2$ = 15.25) and the combination of a positive exercise ECG and abnormal thallium scan ($x^2$ = 6.59) were independent predictors of cardiac events.

D. The majority of effort in the statistical portion of the contract has been spent in data definition and aquisition, and preliminary data screening and analysis. The data has been sub-divided into mortality and 14 areas of risk.

Through meetings with the appropriate investigators at the GRC and elsewhere, definitions of the proper data sets have been accomplished in each of these 15 subsets. The aquisition and processing varies by area of risk. For mortality, cardiology, body composition, personality and nutrition the process is essentially complete. Glucose tolerance, physical activity and blood pressure are in the process of being completed. A few questions remain, which are being resolved, concerning cholesterol, smoking, and family history data. Pulmonary and demographic data are still being defined. Two areas, testosterone and $VO_{2max}$, have been investigated and found to have insufficient data for the analyses contemplated. These areas have therefore been eliminated from further analysis. The analyses are being applied to four basis outcomes:

1. Overall Mortality
2. Cardiovascular Death
3. A "Classical" Definition of Cardiovascular Disease (using stress criteria)
4. MI (including cardiac mortality)

Each of these outcomes is being examined as a function of each of the 12 risk areas separately. In addition, the risk areas are being considered with chronologic age as a co-variate.

Survival curves and distribution of the outcomes on both time in study and age has been completed. Cox's Hazard function analysis, age as a co-variate, has also been completed. These descriptive analyses will comprise the first part of the final presentation.

Within each risk area variables are being defined for intensity, duration and change. Then univariate, followed by multivariate, analyses are being done to define variables to be included in a final overall multivariate analysis using all areas of risk.

The first univariate analyses for the cardiac variables have been completed. These analyses have been reexamined correcting for age. Multivariate analyses of cardiac variables is presently being done.

All definitions are now complete for the personality variables and preliminary analyses have been initiated. Nutrition and glucose tolerance are the next two areas of investigation and are being "prepared" for analysis now.

Significance to Biomedical Research and the Program of the Institute: Resting two-dimensional echocardiography and MUGA scans allow detailed non-invasive analysis of cardiac structure and ventricular function and should expand our findings from M-mode echocardiography. These techniques have helped to elucidate the mechanisms for the diminution in maximal cardiac performance with age and to detect early pathological changes in cardiac muscle function.

Thallium$^{201}$ myocardial imaging permits the non-invasive detection of coronary heart disease in an asymptomatic population. The combination of MUGA, exercise electrocardiography, and thallium scanning represents a new epidemiologic approach to the detection of this disease -- the major cause of death among the elderly. The diagnosis of latent coronary artery disease should allow further insights into the natural history and the effects of various therapeutic interventions on the disease process.

Proposed Course: Currently the contract is in its seventh year and an addition five year extension has been purposed. During the remainder of this fiscal year (84) and the following year, additional thallium and MUGA studies will be performed. Concomitantly, all data will be analyzed with regard to the effect of age on parameters measured. In addition, the multivariate statistical analysis of the significance of risk factors data gathered by various investigators of the Baltimore Longitudinal Study of Aging which are currently being implemented will be continued until the end product is at hand.

In order to determine whether the age-related differences in the mechanisms by which cardiac output is maintained during exercise are related to changes in beta adrenergic responsiveness, we have begun a new study in which BLSA subjects free from CAD by clinical, exercise ECG and thallium scintigraphic criteria perform maximal bicycle exercise (as in our initial study) before and after the intravenous administration of propranolol, 0.15 mg/kg. In the 12 subjects thus far studied, cardiac output at 100 watts was not affected by propranolol; a 16% decrease in heart rate was compensated by a 19% increase in end-diastolic LV volume.

Publications:

Lakatta, E. G.: Some newer perspectives on how the heart ages. In D Pratt (Ed.): Cardiology and Ageing. Stuttgart, Schattauer Verlag, 1983, pp. 53-58.

Rodeheffer, R. J., Gerstenblith, G., Becker, L. C., Fleg, J. L., Weisfeldt, M. L., and Lakatta, E. G.: Exercise cardiac output is maintained with advancing age in healthy human subjects. Circulation, 69: 203-213, 1984.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 AG 02010 06 EDBP

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Followup of Health and Nutrition Examination Survey I (HANES I)

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
*(Name, title, laboratory, and institute affiliation)*

PI: Joan Cornoni-Huntley, Ph.D., M.P.H.
Deputy Associate Director, EDBP, NIA

COOPERATING UNITS *(if any)*

National Center for Health Statistics, Division of Analysis; NCI, Environmental Epidemiology Branch; NHLBI, Epidemiology and Biometry Program; NIADDK; NIMH; and NIAAA.

LAB/BRANCH

Epidemiology Office

SECTION

Epidemiology, Demography, and Biometry Program

INSTITUTE AND LOCATION

NIA, NIH, Bethesda, MD 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
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| .40 | .20 | .20 |

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to design and complete a followup of persons examined in the HANES I to study how factors previously measured relate to the health conditions that have developed since the survey. The three major areas for prediction of outcome are 1) nutrition 2) risk factors for chronic disease and 3) health care utilization. The survey will have a household interview including self-reporting of health conditions, utilization of health servics and behaviorial and social status plus some physical measurements as blood pressure, height, and weight.

The field work data collection component of the initial followup was concluded in April. Only persons located after the interviewers had left the area have received a telephone interview or a questionnaire by mail. Both the National Death Index and the Social Security Death Tape have been used to identify persons who have died. Death certificates have been obtained and proxy interviews completed. Approximately 93 percent of those originally examined in the NHANES I were located. Ninety-four percent of those located were interviewed, producing approximately 85 percent interview rate. Hospital and nursing home data are currently being collected. Information is obtained for all hospitalization and nursing home events during the entire 10-year followup interval. We anticipate approximately 21,000 hospital/nursing home abstracts. Preliminary analyses have begun using interview data tapes for the Northeast, now available at NIH, the Parklawn Computer Center, and at the GRC. A death certificate tape with information on deaths of 389 participants for the Northeast is now available. This does not yet include all deaths since at least 75 other participants from the Northeast are believed to be deceased. Final tapes containing data for the whole sample are expected to be available in October.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 AG 04003 02 EDBP

PERIOD COVERED: October 1, 1983 to September 30, 1984

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.): Dementing Illnesses in the Framingham Heart Study

PRINCIPAL INVESTIGATOR (List other professional personnel on subsequent pages.)
(Name, title, laboratory, and institute affiliation)

PI: Lon R. White, M.D., M.P.H.
Chief, Epidemiology Office, EDBP, NIA

COOPERATING UNITS (if any): NHLBI

LAB/BRANCH: Epidemiology Branch

SECTION: Epidemiology, Demography, and Biometry Program

INSTITUTE AND LOCATION: NIA, NIH, Bethesda, MD 20205

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CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

The Framingham Study population is being utilized for studies on dementia in the elderly. A 2-year interinstitute transfer of funds from NIA to NHLBI was completed in FY 1983 to initiate the study. This was accomplished by the awarding of an NHLBI contract to Boston University School of Medicine. This contract will be extended by a one-year supplementation to the interinstitute agreement (FY 1984).

All study participants currently receive a screening test as part of the biennial examination. Participants suspected of intellectual impairment have been brought back for neurological and neuropsychological evaluation in order to identify individuals suffering from either SDAT or MID. The analysis phase of this part of the study is expected to begin in 1984. In addition, an analysis of the prior neuropsychological test data has been undertaken by NIA and NHLBI staff. These prior results have been used to identify three groups to be the subjects of a followup study: the 212 persons who performed least well (the bottom 10 percent), 212 modal performers (25-75 the percentile range), and 168 of the top (greater than 75th percentile) performers. With the exception of the tests of digit reiteration, there was a substantial decline in all neuropsychological test scores with advancing age. A fourth project examines the influence of hypertension present 2 years prior to neuropsychological testing on the Cycle 14/15 neuropsychological test scores. Preliminary analysis shows no significant adverse effect of hypertension on cognitive function. In contrast, the participants' history of alcohol ingestion appears to be significantly related to performance on the neuropsychological tests.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 AG 04004-02 EDBP

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Healthy Aged--Honolulu Heart Study

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
*(Name, title, laboratory, and institute affiliation)*
PI: Lon R. White, M.D., M.P.H.
Chief, Epidemiology Office, EDBP, NIA

COOPERATING UNITS *(if any)*
Honolulu Heart Program, NHLBI

LAB/BRANCH
Epidemiology Office

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INSTITUTE AND LOCATION
NIA NIH, Bethesda, MD 20205

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CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A professional services contract was awarded to Dr. Benfante to carry out research using the data and facilities of the Honolulu Heart Study. The objective of this study is to define the correlates and predictors of survival and good health in later life. From more than 30 variables examined in multivariate analyses, blood pressure, obesity, cigarette smoking, alcohol consumption, serum glucose, uric acid, and triglyceride were inversely associated with staying healthy while forced vital capacity and birthplace in Japan were directly associated with health. Of these nine variables, blood pressure was the strongest discriminator between healthy status and all categories of disease while cigarette smoking and alcohol consumption were the next most important factors. This study suggests that the use of inidivduals who remain free of disease as a "standard" for health can facilitate the evaluation of risk factors for both total illness and a broad range of specific chronic diseases in a single population.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 AG 01050 05 EDBP

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Age Structure in a Macroeconomic Model of the U.S. Economy

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*

*(Name, title, laboratory, and institute affiliation)* PI: William S. Cartwright, Ph.D., Chief, Demography and Economics Office, EDBP, NIA

COOPERATING UNITS *(if any)*

LAB/BRANCH

Demography and Economics Office

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Epidemiology, Demography, and Biometry Program

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NIA, NIH, Bethesda, MD 20205

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☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A Demographic-Macroeconomic Model of the U.S has been developed. The impact of population aging will be examined on the nation's economy, retirement income system, labor force, and the welfare of the aged. The Demographic Macroeconomic Model represents the integration of eight models - Hudson-Jorgenson Growth Model, Anderson Labor Model, ICF Inc. Population Model, Social Security Model, Private and Public Employees Pension Model, Supplemental Security Income Model, and Medicare Model.

A model has been statistically estimated and an operating simulation program developed. The President's Commission on Pension Policy has used the current model for analytical purposes. Final Reports, Volume 1 and 2, entitled, "A Macroeconomic-Demographic Model of the U.S. Retirement Income System" have been delivered as well as a Research Report. Permission to publish was obtained from the Assistant Secretary of Health and editing of the final reports was completed under a professional services contract.

Publications: Woodruff, TC. Development of a demographic macroeconomic model of the U.S. economy. Chapter 37; and Findings on the impact of pension policy on the economy, Chapter 38 in The Final Report of the President's Commission on Pension Policy, April 1981.

Cartwright, WS (Ed.): The National Institute on Aging, Macroeconomic-Demographic Model. NIH Publ. No. 84-2492, 1984, 140 pp.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 AG 01055 03 EDBP

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Retirement Income System Research with MDM

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
*(Name, title, laboratory, and institute affiliation)* PI: William S. Cartwright, Ph.D., Chief, Demography and Economics Office, EDBP, NIA

COOPERATING UNITS *(if any)*

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Demography and Economics Office

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Epidemiology, Demography, and Biometry Program

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NIA, NIH, Bethesda, MD 20205

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☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The NIA enters into an agreement with the Assistant Secretary for Planning and Evaluation (ASPE) for the purpose of research on pensions, retirement, and labor force as well as issues involved in integration of micro and macroeconomic models. We have supported the revision and reestimation of the labor market model and simulation studies of the labor supply of the elderly.

We have received a detailed grant proposal specifying the work to be undertaken. A new version of the Pension Model has been prepared and delivered to NIA's MDM.

Publications: Retirement Benefit Acceptance and Labor Force Participation; and Connecting the DYNASIM Microsimulation Model and the ICF Macroeconomic-Demographic Model.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 AG 06050 01 EDBP

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Pretesting of the 1984 National Nursing Home Survey

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
*(Name, title, laboratory, and institute affiliation)*

PI: Daniel J. Foley, EDBP, NIA
Evelyn Mathis, NCHS

COOPERATING UNITS *(if any)*

National Center for Health Statistics

LAB/BRANCH

Biometry Office

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NIA, NIH, Bethesda, MD 20205

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☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This interagency agreement covered the cost of work done by NCHS on the pretest of the survey instruments and procedures for the 1985 National Nursing Home Survey (NNHS). The agreement reimbursed the Center for the cost of testing the feasibility of collecting information from relatives of nursing home residents and for collection of information on drugs. Since these are new components to the NNHS, they required the development of "untried" procedures.

The data collection for the pretest is now complete. Although the data analysis is still underway, preliminary results indicate that collection of drug information in this setting is feasible. However, the request for next-of-kin information was denied by many facility administrators and consequently the feasibility of carrying this component over to the main survey is under consideration.